As filed with the Securities and Exchange Commission on May 4, 2006.

Registration No. 333-132912

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 1
to

Form S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

PTC THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**2834**	**04-3416587**
(State or Other Jurisdiction of Incorporation or Organization)	*(Primary Standard Industrial Classification Code No.)*	*(I.R.S. Employer Identification Number)*

100 Corporate Court
South Plainfield, New Jersey 07080-2449
(908) 222-7000
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Stuart W. Peltz, Ph.D.
President and Chief Executive Officer
PTC Therapeutics, Inc.
100 Corporate Court
South Plainfield, New Jersey 07080-2449
(908) 222-7000
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act") please check the following box. o

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

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

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

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 Section 8(a), may determine.

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

PROSPECTUS (Subject to Completion)
Issued May 4, 2006

Shares

COMMON STOCK

PTC Therapeutics, Inc. is offering shares of its common stock. This is our initial public offering, and no public market currently exists for our shares. We anticipate that the initial public offering price will be between $ and $ per share.

We have applied to have our common stock approved for quotation on The Nasdaq National Market under the symbol "PTCT."

Investing in our common stock involves risks. See "Risk Factors" beginning on page 6.

PRICE $ A SHARE

	Price to Public	Underwriting Discounts and Commissions	Proceeds to PTC
Per Share	$	$	$
Total	$	$	$

We have granted the underwriters the right to purchase up to an additional shares of common stock to cover over-allotments.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Morgan Stanley & Co. Incorporated expects to deliver the shares to purchasers on , 2006.

MORGAN STANLEY *JPMORGAN*

PACIFIC GROWTH EQUITIES, LLC

, 2006

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock. In this prospectus, unless otherwise stated or the context otherwise requires, references to "PTC Therapeutics," "we," "us," "our" and similar references refer to PTC Therapeutics, Inc.

Until , 2006, 25 days after the commencement of this offering, all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary may not contain all of the information that is important to you. Before investing in our common stock, you should read this prospectus carefully in its entirety, especially the risks of investing in our common stock that we discuss in the "Risk Factors" section of this prospectus and our financial statements and the related notes beginning on page F-1.

PTC Therapeutics, Inc.

Our Company

We are a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small-molecule drugs that target post-transcriptional control processes. Our lead product development programs are PTC124 for genetic disorders and PTC299 for oncology. We are currently conducting Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy patients with a specific type of genetic mutation. We recently performed an interim analysis of data from 15 patients who have completed our ongoing cystic fibrosis trials and observed results which suggest that PTC124 may have pharmacological activity that addresses the underlying cause of cystic fibrosis in these patients. For PTC299, we commenced a Phase 1a clinical trial in healthy volunteers in April 2006. We have discovered all of our compounds currently under development. We plan to develop these compounds both on our own and through selective collaboration arrangements with leading pharmaceutical and biotechnology companies. We have retained worldwide commercialization rights to PTC124 and PTC299 and recently entered into a collaboration with Schering-Plough Corporation for the development and commercialization of preclinical compounds that we have identified for the potential treatment of hepatitis C.

Post-transcriptional control processes regulate the rate and timing of protein production and are of central importance to proper cellular function. The small-molecule compounds that we are developing are designed to alter post-transcriptional processes and modulate the utilization of messenger RNA, or mRNA, a key intermediate in protein production. We have assembled proprietary technologies and extensive knowledge of post-transcriptional control processes that we apply in our drug discovery and development activities. We believe that systematically targeting these processes represents a new and unexploited approach to drug discovery and development, which has several potential key advantages. These include the potential to use orally available small-molecule drugs to address previously intractable drug targets and to up or down regulate the level of production of a protein of interest. In addition, this approach has the potential to treat a broad range of diseases. Our current pipeline of clinical and preclinical product candidates addresses multiple indications, including genetic disorders, oncology and infectious diseases.

Our Lead Programs

Our three most advanced product development programs are:

- ***PTC124 for genetic disorders.*** We are developing PTC124 for the treatment of patients with genetic disorders that arise as a result of a type of genetic mutation known as a nonsense mutation. Our initial target indications for PTC124 are cystic fibrosis and Duchenne muscular dystrophy in cases in which a nonsense mutation is the cause of the disease. We are currently conducting two Phase 2 clinical trials of PTC124 in patients with cystic fibrosis and one Phase 2 clinical trial of PTC124 in patients with Duchenne muscular dystrophy. We believe that PTC124 is potentially applicable to a broad range of other genetic disorders in which a nonsense mutation is the cause of the disease. We expect to complete our ongoing Phase 2 clinical trials of PTC124 for both cystic fibrosis and Duchenne muscular dystrophy in the second half of 2006.
- ***PTC299 for oncology.*** We are developing PTC299 initially for the treatment of cancer. In preclinical studies, PTC299 directly and potently inhibited the production of vascular endothelial growth factor, or VEGF. VEGF is a protein that plays a central role in tumor growth through the process of new blood vessel formation referred to as angiogenesis. Because PTC299 blocks the production of VEGF,

its activity is different from that of currently available anti-VEGF agents, which typically act by blocking the action of VEGF that has already been produced. In April 2006, we commenced a Phase 1a clinical trial of PTC299 in healthy volunteers in Belgium. If this Phase 1a clinical trial is successful, we plan to initiate a Phase 1b clinical trial of PTC299 in cancer patients in late 2006. PTC299 and related compounds are also potentially applicable to other diseases in which regulating VEGF levels plays a key role, such as age-related macular degeneration.

- ***Hepatitis C development program.*** We have identified a number of small-molecule compounds that, in preclinical tests, inhibited hepatitis C viral protein synthesis and the production of the virus. These compounds target a specific site on the viral mRNA known as an internal ribosomal entry site, or IRES, which is critical to the replication of the hepatitis C virus. We believe that our approach may be complementary to existing therapies and other compounds currently in development for the treatment of hepatitis C.

We are also conducting discovery programs focused on developing new treatments for multiple therapeutic areas, including bacterial infections, anemia and musculoskeletal conditions.

Interim Data from our Phase 2 Cystic Fibrosis Clinical Trials

We are currently conducting two Phase 2 clinical trials of PTC124 in patients with cystic fibrosis caused by nonsense mutations. We expect to enroll at least 18 evaluable patients in each trial. The primary endpoint in both trials is the change in study participants' chloride conductance in respiratory cells as measured by transepithelial potential difference, or TEPD. The primary endpoint of a clinical trial is the outcome measure that is determined to be the most important in assessing whether the objective of the trial has been achieved. TEPD is a common and accepted measure to diagnose and evaluate patients with cystic fibrosis. Cystic fibrosis patients have an abnormal TEPD chloride conductance. We assess the endpoint in three ways: (1) mean change in TEPD chloride conductance; (2) the percentage of patients that achieve a defined improvement in TEPD chloride conductance, referred to as a chloride conductance response; and (3) the percentage of patients with improvement in TEPD chloride conductance into the generally accepted normal range. Participants in the trials take PTC124 in two sequential periods during which they receive PTC124 at specified doses. These periods are referred to as dosing cycles. The first is a lower-dose cycle and the second is a higher-dose cycle. We assess changes in participants' TEPD chloride conductance from the beginning to the end of each dosing cycle.

In March 2006, we conducted an interim analysis of the data from a total of 15 patients who have completed their participation in either of our two trials. In these 15 patients, at both dose levels, we observed statistically significant results in all three ways in which we assessed the endpoint, including mean improvement in TEPD chloride conductance, percentage of patients with a chloride conductance response and percentage of patients with a chloride conductance value improvement into the normal range. Clinical trial results are generally considered to be statistically significant if there is less than a one-in-twenty likelihood that the observed results occurred by chance. We believe that these results suggest that PTC124 may have pharmacological activity that addresses the underlying cause of cystic fibrosis in these patients. We also believe that this is the first time such activity has been observed in a clinical trial of an oral therapy for cystic fibrosis. We also observed improvements in other endpoints, including lung function and weight.

While these interim results do not necessarily predict favorable outcomes from our ongoing Phase 2 clinical trials or any future trial, we believe that these results support our continued development of PTC124 in cystic fibrosis, Duchenne muscular dystrophy and other genetic disorders caused by nonsense mutations.

Our Collaborations

In March 2006, we entered into a collaboration with Schering-Plough for the development and commercialization of compounds in our hepatitis C program. Pursuant to the collaboration, we and Schering-Plough will conduct a joint research program, and Schering-Plough will be responsible for worldwide development and commercialization efforts for any product candidates that are developed. Schering-Plough has made an upfront payment to us of $12.0 million and has agreed to provide funding for our research

activities. In addition, we are eligible to receive more than $200 million in payments if specified development, regulatory and sales milestones are achieved. We are also entitled to royalties on sales of products developed pursuant to the collaboration, with the royalty percentage based on specified thresholds of worldwide net product sales. In addition to our collaboration with Schering-Plough, we have entered into a research collaboration with Bausch & Lomb to identify and potentially license to Bausch & Lomb compounds with anti-angiogenic activity for specified ophthalmic diseases.

Our Proprietary Technologies

We employ several proprietary technologies in our research and development activities. Our principal technology is Gene Expression Modulation by Small Molecules, or GEMS, which we use to identify compounds that increase or decrease protein levels by altering post-transcriptional control processes. GEMS is a screening procedure that is based on our understanding of specific elements of mRNA that are critical for post-transcriptional control. Through the use of GEMS and other proprietary technologies, we have identified compounds that have exhibited desired pharmaceutical activity and side effect profiles in preclinical studies. We believe that these results validate our ability to identify compounds that affect protein levels through post-transcriptional control processes and our ability to optimize these compounds as potential product candidates for their specified indications.

Our Strategy

Our goal is to become a leading pharmaceutical company focused on developing and commercializing small-molecule therapeutics that target post-transcriptional control processes and address unmet medical needs. The key elements of our strategy are to rapidly advance our lead programs; apply our integrated approach to continue to discover and develop small molecules that alter post-transcriptional control processes; build a specialized sales and marketing infrastructure; and selectively establish strategic alliances with leading pharmaceutical and biotechnology companies.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus immediately following this prospectus summary. We have a limited operating history and have not yet commercialized any products. We have incurred substantial operating losses in each year since inception. Our net loss was $22.9 million for the year ended December 31, 2005. As of December 31, 2005, we had a deficit accumulated during the development stage of $92.1 million. We expect to incur significant and increasing net losses for at least the next several years. It is uncertain whether any of our product candidates under development will become effective treatments. All of our product candidates are undergoing clinical trials or are in earlier stages of development, and failure is common and can occur at any stage of development. None of our drug candidates has received regulatory approval for commercialization, and we do not expect that any drugs resulting from our or our collaborators' research and development efforts will be commercially available for a number of years, if at all. We may never receive any product sales revenues or achieve profitability.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in March 1998. Our principal executive offices are located at 100 Corporate Court, South Plainfield, New Jersey 07080-2449, and our telephone number is (908) 222-7000. Our website address is *www.ptcbio.com*. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

THE OFFERING

Common stock we are offering	shares
Common stock to be outstanding after this offering	shares
Over-allotment option	shares
Use of Proceeds	We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ million if the underwriters exercise their over-allotment option in full, assuming an initial public offering price of $ per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. We expect to use most of the net proceeds from this offering to fund clinical trials, preclinical testing and other research and development activities and the balance for working capital and other general corporate purposes. See "Use of Proceeds."
Risk Factors	You should read the "Risk Factors" section of this prospectus for a discussion of the factors to consider carefully before deciding to purchase any shares of our common stock.
Proposed Nasdaq National Market symbol	PTCT

The number of shares of our common stock to be outstanding immediately after this offering is based on 11,889 shares of common stock outstanding as of March 15, 2006 and an additional 13,504,722 shares of common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering. The number of shares of common stock to be outstanding after this offering excludes:

- 2,340,715 shares of common stock issuable upon the exercise of stock options outstanding as of March 15, 2006 at a weighted average exercise price of $2.40 per share;
- 277,151 shares of common stock issuable upon the exercise of warrants outstanding as of March 15, 2006 at a weighted average exercise price of $17.86 per share;
- an aggregate of shares of common stock reserved for future issuance under our 2006 equity incentive plan as of the closing of this offering; and
- an aggregate of shares of common stock reserved for future issuance under our 2006 employee stock purchase plan as of the closing of this offering.

Unless otherwise noted, all information in this prospectus assumes:

- no exercise of the outstanding options or warrants described above;
- no exercise by the underwriters of their option to purchase up to shares of common stock to cover over-allotments; and
- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 13,504,722 shares of common stock upon the closing of this offering.

SUMMARY FINANCIAL DATA

The following is a summary of our financial information. You should read this information together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus.

The pro forma as adjusted balance sheet data set forth below gives effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 13,504,722 shares of common stock upon the closing of this offering and to our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

Please see note 2 to our financial statements appearing at the end of this prospectus for an explanation of the method used to calculate the net loss per share, the pro forma net loss per share and the number of shares used in the computation of per share amounts.

	Year Ended December 31,			Period from March 31, 1998 (Inception) to December 31, 2005
	2003	2004	2005	
	(in thousands, except share and per share data)			
Statements of Operations Data:				
Revenues	$ 756	$ 1,606	$ 4,967	$ 7,669
Operating expenses:				
Research and development	17,695	20,070	21,123	76,970
General and administrative	4,693	6,023	7,944	27,231
Total operating expenses	22,388	26,093	29,067	104,201
Loss from operations	(21,632)	(24,487)	(24,100)	(96,532)
Interest income	317	579	854	3,998
Interest expense	(358)	(184)	(141)	(1,007)
Loss before tax benefit	(21,673)	(24,092)	(23,387)	(93,541)
Tax benefit	235	451	479	1,397
Loss applicable to common stockholders	$ (21,438)	$ (23,641)	$ (22,908)	$ (92,144)
Basic and diluted loss per share applicable to common stockholders	$ (315,259)	$ (347,670)	$ (9,925)	
Shares used to compute basic and diluted loss per share applicable to common stockholders	68	68	2,308	
Pro forma basic and diluted net loss per common share (unaudited)			$ (2.11)	
Shares used to compute pro forma basic and diluted net loss per common share (unaudited)			10,831,634	

	As of December 31, 2005	
	Actual	Pro Forma As Adjusted (unaudited)
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents and short-term investments	$ 37,840	
Working capital	34,331	
Total assets	43,974	
Long-term debt, net of current portion	804	
Deficit accumulated during the development stage	(92,144)	
Total stockholders' equity	38,401	

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information included in this prospectus, including the financial statements and related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, they may materially harm our business, prospects, financial condition and results of operations. In this event, the market price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $22.9 million for the year ended December 31, 2005. As of December 31, 2005, we had a deficit accumulated during the development stage of $92.1 million. To date, we have financed our operations primarily through private placements of our preferred stock and, to a lesser extent, through a variety of governmental grant programs and through financial support from advocacy groups and foundations in the disease areas addressed by our product candidates. We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed development of any drugs. We expect to continue to incur significant and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially as we:

- continue our ongoing Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations and conduct potential later stage clinical trials of PTC124 if our Phase 2 trials are successful;
- initiate and pursue clinical trials of PTC299 for the treatment of cancer;
- continue the research and development of our other product candidates;
- seek to discover and develop additional product candidates;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- establish a sales and marketing infrastructure to commercialize products for which we may obtain regulatory approval; and
- add operational, financial and management information systems and personnel, including personnel to support our product development efforts and our obligations as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing drugs with significant market potential. This will require us to be successful in a range of challenging activities, including discovering product candidates, successfully completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of these activities. We may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the market price of our common stock would also cause you to lose all or a part of your investment.

We will need substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we continue our Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations, commence additional clinical trials of PTC124 if our ongoing Phase 2 clinical trials are successful, commence additional clinical trials of PTC299 for the treatment of cancer and continue the research activities in our hepatitis C virus program in collaboration with Schering-Plough. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, securing commercial quantities of product from our manufacturers and distribution. We will need substantial additional funding and may be unable to raise capital when needed or on attractive terms, which would force us to delay, reduce or eliminate our research and development programs or commercialization efforts.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, short-term investments and research funding that we expect to receive under our collaborations, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements until . Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical trials of PTC124 and PTC299;
- the success of our hepatitis C virus collaboration with Schering-Plough;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the extent to which we acquire or invest in businesses, products and technologies; and
- our ability to establish and maintain collaborations.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through public or private equity offerings and debt financings, corporate collaboration and licensing arrangements and grants from patient advocacy groups, foundations and government agencies. If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences that are not favorable to us or our stockholders. If we raise additional funds through collaboration and licensing arrangements with third parties, it may be necessary to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a development-stage company. We commenced active operations in 2000. Our operations to date have been limited to organizing and staffing our company, acquiring, developing and securing our technology and undertaking preclinical studies and limited clinical trials of our most advanced product candidates. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, obtain

regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Risks Related to the Development and Commercialization of Our Product Candidates

We depend heavily on the success of our most advanced product candidates, particularly PTC124 and PTC299. All of our product candidates are still in preclinical and clinical development. Clinical trials of our product candidates may not be successful. If we are unable to commercialize PTC124 or PTC299, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of our most advanced product candidates, PTC124 for the treatment of genetic disorders and PTC299 for the treatment of cancer. Our ability to generate product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and eventual commercialization of these product candidates. The success of our product candidates will depend on several factors, including the following:

- successful completion of clinical trials;
- successful completion of additional preclinical studies, such as the additional toxicity study of PTC124 that we are conducting in rats, at the request of the United States Food and Drug Administration, or FDA;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States;
- establishing commercial manufacturing arrangements with third-party manufacturers;
- launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payors;
- competition from other therapies; and
- a continued acceptable safety profile of the product following approval.

Interim results from a clinical trial are not indicative of the successful outcome of that trial and the results of early stage clinical trials do not ensure success in later stage clinical trials.

Our efforts to commercialize all of our product candidates are at an early stage. We are currently conducting Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations. We expect to complete these Phase 2 clinical trials in 2006. In April 2006, we commenced a Phase 1a clinical trial of PTC299 in healthy volunteers in Belgium. If this Phase 1a clinical trial is successful, we plan to initiate a Phase 1b clinical trial of PTC299 in late 2006 in patients with advanced solid tumors whose disease has progressed during therapy or for whom there is no effective therapy available. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, the interim results to date in our Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis caused by nonsense mutations are based on data from only 15 patients and include patients from both trials. Data from additional patients enrolled in these trials may be less favorable than the data observed to date. We cannot assure you that either trial will ultimately be successful. In addition, the results from these 15 patients have only become available recently. New information regarding the safety and efficacy of PTC124 may arise from

our continuing analysis of the data that may be less favorable than the data observed to date. In these Phase 2 trials, patients take PTC124 for two-week periods. PTC124 may not be found to be effective or safe when taken for longer periods.

In addition, the primary endpoints in our Phase 2 clinical trials of PTC124 are based on pharmacodynamic markers of changes in the disease state. For example, in our Phase 2 cystic fibrosis trials, we are using chloride conductance as measured by TEPD as a pharmacodynamic marker of changes in a cystic fibrosis patient's disease state. We anticipate that the primary endpoints in later stage clinical trials of PTC124 will be different than the endpoints in our Phase 2 trials. We expect that primary endpoints for future clinical trials of PTC124 in cystic fibrosis would include longer-term clinical measures of lung function and that primary endpoints for future clinical trials of PTC124 in Duchenne muscular dystrophy would include clinical measures of muscle function. As such, the results of our Phase 2 clinical trials are not necessarily indicative of the results we may obtain in later stage clinical trials. It may also be more difficult for us to achieve these endpoints than those we are using in our Phase 2 clinical trials.

Even if our early phase clinical trials are successful, we will need to conduct additional clinical trials in larger numbers of patients taking the drug for longer periods for all of our product candidates before we are able to seek approvals to market and sell these product candidates from the FDA and similar regulatory authorities outside the United States. Similarly, even if clinical trials of a product candidate are successful in one indication, clinical trials of that product candidate for other indications may be unsuccessful. If we are not successful in commercializing any of our lead product candidates, or are significantly delayed in doing so, our business will be materially harmed.

If our preclinical studies do not produce positive results or if our clinical trials are delayed, we may experience delays, incur additional costs and ultimately be unable to commercialize our product candidates.

Before obtaining regulatory approval for the sale of our product candidates, we must conduct, at our own expense, extensive preclinical tests to demonstrate the safety of our product candidates in animals and clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, preclinical testing and the clinical trial process that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- our preclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical testing or clinical trials or we may abandon projects that we expect to be promising;
- the number of patients required for our clinical trials may be larger than we anticipate, enrollment in our clinical trials may be slower than we currently anticipate, or participants may drop out of our clinical trials at a higher rate than we anticipate, any of which would result in significant delays;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner;
- we might have to suspend or terminate our clinical trials if the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of our clinical trials may be greater than we anticipate;

- the supply or quality of our product candidates or other materials necessary to conduct our clinical trials may be insufficient or inadequate because we do not currently have any agreements with third-party manufacturers for the long-term commercial supply of any of our product candidates; and
- the effects of our product candidates may not be the desired effects or may include undesirable side effects or the product candidates may have other unexpected characteristics.

In particular, we recently commenced Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations. Both of these indications are characterized by relatively small patient populations, which may result in slow enrollment of clinical trial participants. In addition, we may experience delays in agreeing to the endpoints for later stage clinical trials of PTC124 with the FDA and similar regulatory authorities outside the United States.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete our clinical trials or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not be able to obtain marketing approval;
- obtain approval for indications that are not as broad as intended; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or approvals. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, if at all. Significant preclinical or clinical trial delays also could shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to commercialize our products or product candidates.

If serious adverse or inappropriate side effects are identified during the development of our product candidates, we may need to abandon our development of some of our product candidates.

All of our product candidates are in an early stage of development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. If the effects of our product candidates include undesirable side effects or have characteristics that are unexpected, we may need to abandon our development of those product candidates.

In our preclinical testing of PTC124, we noted inflammatory cells in the adrenal glands of some dogs that were treated with PTC124. The clinical implications, if any, of this observation are unknown. We may need to assess adrenal function in humans receiving PTC124 or perform other tests if required by the FDA or other regulatory authorities. Also in our preclinical testing of PTC124, some rats developed brown fat tumors, tumors of the mammary glands and tumors of the testes. It was not clear whether the non-brown fat tumors were caused by PTC124. Brown fat tumors can occur in small animals, including rodents, but are extremely rare in humans. Other drugs known to cause growth of brown fat tumors in rats have not been observed to cause similar tumors in humans. However, at the request of the FDA, we are conducting an additional six-month toxicity study of PTC124 in rats. If the results of this study are unfavorable, our ability to continue the development of PTC124 may be adversely affected.

In one of our Phase 1 clinical trials of PTC124, we observed modest elevations of liver enzymes in some subjects. These elevated enzyme levels did not require cessation of PTC124 administration, and enzyme levels typically normalized after completion of the treatment phase. We did not observe any increases in bilirubin, which can be associated with serious harm to the liver. In the 15 participants we have evaluated to date on our Phase 2 clinical trials for cystic fibrosis, we did not observe any meaningful elevations in liver enzymes or bilirubin. If we were to observe elevations in liver enzymes in patients in our ongoing or potential future

clinical trials of PTC124, we may be unable to continue the development of the product candidate. Alternatively, we may be required to instruct physicians to frequently monitor patients for liver enzyme abnormalities, which could be an impediment to the use of PTC124 because of concerns related to its safety and convenience.

Our focus on the discovery and development of product candidates that target post-transcriptional control processes is unproven, and we do not know whether we will be able to develop any products of commercial value.

Our scientific approach focuses on the discovery and development of product candidates that target post-transcriptional control processes. While a number of commonly used drugs and a growing body of research validate the importance of post-transcriptional control processes in the origin and progression of a number of diseases, no existing drugs have been specifically designed to alter post-transcriptional control processes in the same manner as our lead product candidates. As a result, we cannot be certain that our focus on targeting these processes will result in the discovery and development of commercially viable drugs that safely and effectively treat genetic disorders, cancer, hepatitis C or other diseases. In addition, even if we are successful in developing and receiving regulatory approval for a commercially viable drug that treats an approved indication by targeting a particular post-transcriptional control process, we cannot be certain that we will also be able to receive regulatory approval for additional indications. Nor can we be certain that we will be able to receive regulatory approval for product candidates that target different post-transcriptional control processes. If we fail to develop and commercialize viable drugs, we will not achieve commercial success.

The commercial success of any product candidates that we may develop, including PTC124 and PTC299, will depend upon the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community.

Any products that we bring to the market, including PTC124 and PTC299 if they receive marketing approval, may not gain market acceptance by physicians, patients, healthcare payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the prevalence and severity of any side effects;
- the efficacy and potential advantages over alternative treatments;
- the ability to offer our product candidates for sale at competitive prices;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate product revenues.

We do not have a sales or marketing organization and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. Currently, we plan to build a focused specialty sales and marketing infrastructure to market or co-promote some of our product candidates if and when they are approved. There are risks involved with establishing our own sales and marketing capabilities, as well as in entering into arrangements with third parties to perform these services. For example, developing a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing

capabilities is delayed or prohibited as a result of FDA requirements or other reasons, we would incur related expenses too early relative to the product launch. This may be costly, and our investment would be lost if we cannot retain our sales and marketing personnel. In addition, even if we establish our own sales force and marketing capabilities, our sales force and marketing teams may not be successful in commercializing our products.

If we are unable to obtain adequate reimbursement from governments or third-party payors for any products that we may develop or if we are unable to obtain acceptable prices for those products, our revenues and prospects for profitability will suffer.

Our revenues and profits will depend heavily upon the availability of adequate reimbursement for the use of our approved product candidates from governmental and other third-party payors, both in the United States and in other markets. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining reimbursement approval for a product from each government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement. Even when a payor determines that a product is eligible for reimbursement, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA or comparable authorities. In addition, there is a risk that full reimbursement may not be available for high priced products. Moreover, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. A primary trend in the United States healthcare industry and elsewhere is toward cost containment. We expect recent changes in the Medicare program and increasing emphasis on managed care to continue to put pressure on pharmaceutical product pricing.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products

caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We have product liability insurance that covers our clinical trials up to a $5.0 million annual aggregate limit and subject to a per claim deductible. The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any products. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost and we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise.

We face substantial competition which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. For example, several large pharmaceutical and biotechnology companies currently market and sell products to manage the symptoms and side effects of cystic fibrosis. These products include Chiron Corporation's TOBI and Genentech, Inc.'s Pulmozyme. Although there are no products currently approved to treat the root causes of cystic fibrosis, we could also face future potential competition from pharmaceutical companies seeking to develop drugs aimed at modulating CFTR function, including programs of Alnylam Pharmaceuticals, Inc. and Vertex Pharmaceuticals Incorporated. Although there are currently no approved therapeutics to treat the root causes of Duchenne muscular dystrophy, we are aware of early stage gene therapy programs of third parties targeting Duchenne muscular dystrophy, which if successful would compete with PTC124 if it is approved for the treatment of Duchenne muscular dystrophy. If approved for the treatment of cancer, we expect that PTC299 would compete with other anti-angiogenesis therapies. These include Genentech's Avastin, Bayer's and Onyx's Nexavar and Pfizer Inc.'s Sutent. We are also aware of numerous other anti-angiogenesis cancer therapies in development by third parties, including the VEGF Trap, which is in development by Sanofi-Aventis and Regeneron. There are numerous product candidates for the treatment of HCV in clinical development. These include product candidates of Idenix Pharmaceuticals, Inc. and Vertex Pharmaceuticals.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We believe that many competitors are attempting to develop therapeutics for many of our target indications, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and

marketing approved products than we do. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs or advantageous to our business.

Our business activities involve the use of hazardous materials, which require compliance with environmental and occupational safety laws regulating the use of such materials. If we violate these laws, we could be subject to significant fines, liabilities or other adverse consequences.

Our research and development programs involve the controlled use of hazardous materials. Accordingly, we are subject to federal, state and local laws governing the use, handling and disposal of these materials. Although we believe that our safety procedures for handling and disposing of these materials comply in all material respects with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In addition, our collaborators may not comply with these laws. In the event of an accident or failure to comply with environmental laws, we could be held liable for damages that result, and any such liability could exceed our assets and resources. We maintain liability insurance for some of these risks, but our policy excludes pollution and has a coverage limit of $5.0 million.

Risks Related to Our Dependence on Third Parties

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, and clinical development and commercialization of our product candidates could be delayed, prevented or impaired.

We do not own or operate manufacturing facilities for clinical or commercial production of our product candidates. We have limited personnel with experience in drug manufacturing and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. Our strategy is to outsource all manufacturing of our product candidates and products to third parties.

We do not currently have any agreements with third-party manufacturers for the long-term commercial supply of any of our product candidates. To date, we have obtained our supply of the bulk drug substance for both PTC124 and PTC299 from one third-party manufacturer. We engaged a second manufacturer to provide the fill and finish services for the finished product that we are using in our ongoing Phase 2 clinical trials of PTC124 and our Phase 1a clinical trial of PTC299. We are in the process of negotiating an agreement with a new manufacturer for the supply of bulk drug substance for our future clinical trials of PTC124 and PTC299. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms. Even if we conclude these agreements, the manufacturers of each product candidate will be our sole suppliers of our product candidates for a significant period of time. These are commonly referred to as single source suppliers.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates or products ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party because of factors beyond our control; and
- the possible termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

Our manufacturers may not be able to comply with current good manufacturing practice, or cGMP, regulations or other regulatory requirements or similar regulatory requirements outside the United States. Our manufacturers are subject to unannounced inspections by the FDA, state regulators and similar regulators outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil

penalties, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. If the third parties that we engage to manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize any products that receive regulatory approval on a timely and competitive basis.

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

We do not independently conduct clinical trials for our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Our reliance on these third parties for clinical development activities reduces our control over these activities. We are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We may not be successful in maintaining or establishing collaborations, which could adversely affect our ability to discover, develop and, particularly in international markets, commercialize products.

For each of our product candidates, we plan to evaluate the merits of retaining commercialization rights for ourselves or entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies, such as our collaborations with Schering-Plough and Bausch & Lomb. We generally plan to seek collaborators for the later stage development and commercialization of product candidates that have high potential development costs or that are directed at indications for which a potential collaborator has a particular expertise or that involve markets that can be served more effectively by a large sales and marketing organization. We also expect to seek to establish collaborations for the sales, marketing and distribution of our products outside the United States. If we are unable to reach agreements with suitable collaborators, we may fail to meet our business objectives for the affected product or program. We face, and will continue to face, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are

complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements. The terms of any collaborations or other arrangements that we establish may not be favorable to us.

Any collaboration that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. It is likely that our collaborators will have significant discretion in determining the efforts and resources that they will apply to these collaborations. In particular, the successful development of a product candidate from our hepatitis C virus program will initially depend on the success of our research collaboration with Schering-Plough and whether Schering-Plough declares one or more of the compounds discovered under the collaboration as development candidates. Thereafter, Schering-Plough will have significant discretion in the development and commercialization of any such development candidate. Schering-Plough may choose not to pursue further development and commercialization of such development candidates based on many factors outside of our control, including changes in Schering-Plough's strategic focus or available funding, or external factors such as a merger or acquisition that diverts resources or creates competing priorities.

The risks that we are subject to in our current collaborations, and anticipate being subject to in future collaborations, include the following:

- our collaboration agreements are likely to be for fixed terms and subject to termination by our collaborators in the event of a material breach or lack of scientific progress by us;
- our collaborators are likely to have the first right to maintain or defend our intellectual property rights and, although we would likely have the right to assume the maintenance and defense of our intellectual property rights if our collaborators do not, our ability to do so may be compromised by our collaborators' acts or omissions; and
- our collaborators may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. For example, Schering-Plough has the right to terminate our hepatitis C virus collaboration at any time after the third anniversary of the agreement upon prior written notice. Schering-Plough can also terminate the collaboration if it has not accepted a development candidate within two years of the effective date of the agreement. Such terminations or expirations would adversely affect us financially and could harm our business reputation.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain protection for the intellectual property relating to our technology and products, the value of our technology and products will be adversely affected.

Our success will depend in large part on our ability to obtain and maintain protection in the United States and other countries for the intellectual property covering or incorporated into our technology and products. The patent situation in the field of biotechnology and pharmaceuticals generally is highly uncertain and involves complex legal and scientific questions. We may not be able to obtain additional issued patents relating to our technology or products. Even if issued, patents issued to us or our licensors may be challenged, narrowed, invalidated, held to be unenforceable or circumvented, which could limit our ability to stop competitors from marketing similar products or limit the length of term of patent protection we may have for our products. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

Our patents also may not afford us protection against competitors with similar technology. Because patent applications in the United States and many other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in our or their issued patents or pending patent applications, or that we

or they were the first to file for protection of the inventions set forth in these patent applications. If a third party has also filed a U.S. patent application covering our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the U.S. Patent Office to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts could be unsuccessful, resulting in a loss of our U.S. patent position.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a number of license agreements and expect to enter into additional licenses in the future. Our existing licenses impose, and we expect that future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

In addition to patented technology, we rely upon unpatented proprietary technology, processes and know-how. We seek to protect our unpatented proprietary information in part by confidentiality agreements with our employees, consultants and third parties. These agreements may be breached and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently developed by competitors. If we are unable to protect the confidentiality of our proprietary information and know-how, competitors may be able to use this information to develop products that compete with our products, which could adversely impact our business.

If we infringe or are alleged to infringe intellectual property rights of third parties, it will adversely affect our business.

Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, may infringe or be accused of infringing one or more claims of an issued patent or may fall within the scope of one or more claims in a published patent application that may subsequently issue and to which we do not hold a license or other rights. Third parties may own or control these patents or patent applications in the United States and abroad. These third parties could bring claims against us or our collaborators that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit.

With respect to PTC124, we are aware of published U.S. and international patent applications that purport to disclose or contain claims to chemical scaffolds that are sufficiently broad that they could be read to encompass PTC124, even though none of these applications specifically discloses PTC124. Although none of these published applications has issued, if a U.S. patent containing compound claims covering PTC124 is issued to one or more of these third parties, one or more of these third parties may bring a patent infringement or other legal proceeding against us regarding PTC124. We believe that the claims of these patent applications that could be read to encompass PTC124, including the allowed claims in a U.S. application, were they to issue in their current form, would likely be held to be invalid. In order to successfully challenge the validity of any issued U.S. patent, we would need to overcome a presumption of validity. This burden is a high one requiring us to present clear and convincing evidence as to the invalidity of these claims. There is no assurance that a court would find these claims to be invalid.

With respect to PTC299, we are aware of published U.S. and international patent applications that purport to disclose or contain claims to chemical scaffolds that are sufficiently broad that they could be read to encompass PTC299, even though none of these applications specifically discloses PTC299. Although none of these published applications has issued, if a U.S. patent containing compound claims covering PTC299 is

issued to one or more of these third parties, one or more of these third parties may bring a patent infringement or other legal proceeding against us regarding PTC299. We anticipate that we would challenge the validity of such a patent claim.

In addition, we believe that our testing of both PTC124 and PTC299 in clinical trials for the purpose of seeking FDA approval would be a valid defense against any infringement claims in the United States based on the availability of a statutory exemption. However, there can be no assurance that our interpretation of the statutory exemption would be upheld.

If any patents issued from the patent applications described above were found to be valid and we were found to infringe any of them, or any other patent rights of third parties, or in order to avoid potential claims, we or our potential future collaborators may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we or our collaborators are unable to enter into licenses on acceptable terms. This could harm our business significantly.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other proceedings, including interference proceedings declared by the United States Patent and Trademark Office and opposition proceedings in the European Patent Office, regarding intellectual property rights with respect to our products and technology. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We try to ensure that our employees do not use the proprietary information or know-how of others in their work for us. However, we may be subject to claims that we or these employees have inadvertently or otherwise used or disclosed intellectual property, trade secrets or other proprietary information of any such employee's former employer. Litigation may be necessary to defend against these claims and, even if we are successful in defending ourselves, could result in substantial costs to us or be distracting to our management. If we fail to defend any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel.

Risks Related to Regulatory Approval of Our Product Candidates

If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, including PTC124 for the treatment of genetic disorders and PTC299 for the treatment of cancer, and the activities associated with their development and commercialization, including their testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate will prevent us from commercializing the product candidate. We have not received regulatory approval to market any of our product candidates in any jurisdiction. We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each

therapeutic indication to establish the product candidate's safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. Our future products may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

We may not be able to obtain orphan drug exclusivity for our product candidates. If our competitors are able to obtain orphan drug exclusivity for their products that are the same drug as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. We have obtained orphan drug designations from the FDA and from the European Medicines Agency, or EMEA, for our product candidate PTC124 for the treatment of cystic fibrosis caused by nonsense mutations and for the treatment of Duchenne muscular dystrophy caused by nonsense mutations. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMEA or the FDA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. For a drug composed of small molecules, the FDA defines "same drug" as a drug that contains the same active molecule and is intended for the same use. Obtaining orphan drug exclusivity for PTC124 for these indications, both in the United States and in Europe, may be important to the product candidate's success. If a competitor obtains orphan drug exclusivity for a product competitive with PTC124 before we do and if the competitor's product is the same drug as ours, we would be excluded from the market. Even if we obtain orphan drug exclusivity for PTC124 for these indications, we may not be able to maintain it. For example, if a competitive product that is the same drug as our product candidate is shown to be clinically superior to our product candidate, any orphan drug exclusivity we have obtained will not block the approval of such competitive product.

The fast track designation for PTC124 may not actually lead to a faster development or regulatory review or approval process.

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. We have obtained a fast track designation from the FDA for PTC124 for the treatment of both cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations. However, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw our fast track designation if the FDA believes that the designation is no longer supported by data from our clinical development program. Our fast track designation does not guarantee that we will qualify for or be able to take advantage of the FDA's expedited review procedures.

Any product for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and comparable regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on such products, manufacturers or manufacturing processes;
- warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall;
- fines;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our products abroad.

We intend to have our products marketed outside the United States. In order to market our products in the European Union and many other jurisdictions, we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA approval. The regulatory approval process outside the United States may include all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Dr. Stuart W. Peltz, our co-founder, President and Chief Executive Officer, and the other principal members of our executive and scientific teams. The loss of the services of any of these

persons might impede the achievement of our research, development and commercialization objectives. We do not maintain "key person" insurance on Dr. Peltz or on any of our other executive officers.

Recruiting and retaining qualified scientific personnel, clinical personnel and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the inexperience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock and This Offering

After this offering, our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to stockholders for approval.

When this offering is completed, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately % of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, will control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;

- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

We expect the initial public offering price of our common stock to be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent outstanding options or warrants are exercised, you will incur further dilution. Based on an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, you will experience immediate dilution of $ per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the assumed initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately % of the aggregate price paid by all purchasers of our stock but will own only approximately % of our common stock outstanding after this offering.

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we have applied to have our common stock approved for quotation on The Nasdaq National Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares or at all.

If our stock price is volatile, purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their

common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts' reports or recommendations;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We have never paid cash dividends on our capital stock and we do not anticipate paying any cash dividends in the foreseeable future.

We have paid no cash dividends on our capital stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding shares of common stock based on the number of shares outstanding as of March 15, 2006. This includes the shares that we are selling in this offering, which may be resold in the public market immediately. Of the remaining shares, shares are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold after the offering as described in the "Shares Eligible for Future Sale" section of this prospectus. Moreover, after this offering, holders of an aggregate of shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to the lock-up agreements described in the "Underwriters" section of this prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- our plans to develop and commercialize PTC124 and PTC299;
- our collaborations with Schering-Plough and Bausch & Lomb;
- our ongoing and planned discovery programs, preclinical studies and clinical trials;
- the potential benefits of our existing collaboration agreements and our ability to enter into selective additional collaboration arrangements;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our ability to quickly and efficiently identify and develop product candidates;
- the extent to which our scientific approach may potentially address a broad range of diseases across multiple therapeutic areas;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of common stock in this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and offering expenses payable by us. A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) our net proceeds from this offering by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions. If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds to us from this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

We intend to use the net proceeds from this offering as follows:

- approximately $ million to fund a portion of our development activities for PTC124, including the ongoing Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy and potential later stage clinical trials if our Phase 2 trials are successful;
- approximately $ million to fund a portion of our development activities for PTC299, including our Phase 1a clinical trial in healthy volunteers and our planned Phase 1b clinical trial in cancer patients;
- approximately $ million to fund research and development for our discovery programs; and
- the balance, if any, to fund working capital, capital expenditures and other general corporate purposes, which may include the acquisition or licensing of complementary technologies, products or businesses.

This expected use of net proceeds of this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures depend on numerous factors, including the ongoing status of and results from clinical trials and other studies for PTC124 and PTC299, as well as the development of our preclinical product pipeline, any collaborations we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We do not expect the net proceeds from this offering and our other available funds to be sufficient to fund the completion of the development of our lead product candidates, and we expect that we will need to raise additional funds prior to being able to market any products. We have no current plans, agreements or commitments for any material acquisitions or licenses of any technologies, products or businesses.

Pending use of the proceeds from this offering, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and short-term investments and our capitalization as of December 31, 2005:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 13,504,722 shares of common stock upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

The pro forma information below is illustrative only and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing at the end of this prospectus.

	As of December 31, 2005		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands) (unaudited)		
Cash and cash equivalents and short-term investments(1)	$ 37,840	$ 37,840	$
Long-term debt, net of current portion	$ 804	$ 804	$
Stockholders' equity:			
Series A convertible preferred stock, par value $0.001 per share; 750,000 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	750	—	
Series B convertible preferred stock, par value $0.001 per share; 187,500 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	365	—	
Series C convertible preferred stock, par value $0.001 per share; 6,295,000 shares authorized and 6,000,000 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	14,117	—	
Series D convertible preferred stock, par value $0.001 per share; 13,800,000 shares authorized and 13,095,769 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	39,282	—	
Series E convertible preferred stock, par value $0.001 per share; 128,242,850 shares authorized and 125,740,607 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	49,048	—	
Series E-2 convertible preferred stock, par value $0.001 per share; 4,132,232 shares authorized and 3,670,138 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	26,511	—	
Preferred Stock, par value $0.001 per share; no shares authorized, issued or outstanding, actual and pro forma; shares authorized and no shares issued or outstanding, pro forma as adjusted			
Common stock, par value $0.001 per share; 18,228,538 shares authorized, actual and pro forma; 6,943 shares issued and outstanding, actual; 13,511,665 shares issued and outstanding, pro forma; shares authorized and shares issued and outstanding, pro forma as adjusted	—	14	
Additional paid-in capital(1)	506	130,565	
Accumulated other comprehensive loss	(34)	(34)	
Deficit accumulated during the development stage	(92,144)	(92,144)	
Total stockholders' equity(1)	38,401	38,401	
Total capitalization(1)	$ 39,205	$ 39,205	$

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) each of cash and cash equivalents and short-term investments, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions.

The table above does not include:

- 2,064,958 shares of common stock issuable upon exercise of options outstanding as of December 31, 2005 at a weighted average exercise price of $2.28 per share;
- 277,151 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2005 at a weighted average exercise price of $17.86 per share;
- an aggregate of shares of common stock reserved for future issuance under our 2006 equity plan as of the closing of this offering; and
- an aggregate of shares of common stock reserved for future issuance under our 2006 employee stock purchase plan as of the closing of this offering.

DILUTION

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the pro forma net tangible book value per share of our common stock after this offering.

The historical net tangible book value of our common stock as of December 31, 2005 was approximately $ million or $ per share, based on 6,943 shares of common stock outstanding as of December 31, 2005. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of common stock outstanding.

Our pro forma net tangible book value as of December 31, 2005 was approximately $ million, or $ per share of common stock. Pro forma net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the pro forma number of shares of common stock outstanding after giving effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 13,504,722 shares of common stock upon the closing of this offering.

After giving effect to our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, less the estimated underwriting discounts and commissions and offering expenses payable by us, our pro forma net tangible book value as of December 31, 2005 would have been approximately $ million or $ per share. This represents an immediate increase in pro forma net tangible book value of $ per share to our existing stockholders and immediate dilution in pro forma net tangible book value of $ per share to new investors purchasing common stock in this offering at the initial public offering price. Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by a new investor. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$
Historical net tangible book value per share as of December 31, 2005	$	
Increase attributable to the conversion of outstanding preferred stock		
Pro forma net tangible book value per share as of December 31, 2005		
Increase per share attributable to new investors		
Pro forma net tangible book value per share after this offering		
Dilution per share to new investors		$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) our pro forma net tangible book value after the offering by approximately $ million, our pro forma net tangible book value per share after this offering by approximately $ and dilution per share to new investors by approximately $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions.

If the underwriters exercise their over-allotment option or if any shares are issued in connection with outstanding options or warrants, you will experience further dilution.

The following table summarizes as of December 31, 2005 the number of shares purchased from us after giving effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 13,504,722 shares of common stock upon the closing of this offering, the total consideration paid and the average price per share paid, or to be paid, to us by existing stockholders and by new investors in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price per Share
	Number	Percentage	Amount	Percentage	
Existing stockholders		%		%	$
New investors					
Total		100%		$ 100%	

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the total consideration paid by new investors by $ million and increase (decrease) the percentage of total consideration paid by new investors by approximately %, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The table above is based on 6,943 shares of common stock outstanding as of December 31, 2005 and an additional 13,504,722 shares of common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering and excludes:

- 2,064,958 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2005 at a weighted average exercise price of $2.28 per share;
- 277,151 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2006 at a weighted average exercise price of $17.86 per share;
- an aggregate of shares of common stock reserved for future issuance under our 2006 equity plan as of the closing of this offering; and
- an aggregate of shares of common stock reserved for future issuance under our 2006 employee stock purchase plan as of the closing of this offering.

If the underwriters exercise their over-allotment option in full, the following will occur:

- the percentage of shares of common stock held by existing stockholders will decrease to approximately % of the total number of shares of our common stock outstanding after this offering; and
- the pro forma as adjusted number of shares held by new investors will be increased to , or approximately %, of the total pro forma as adjusted number of shares of our common stock outstanding after this offering.

SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statements of operations data for the years ended December 31, 2003, 2004 and 2005 and for the period from March 31, 1998 (inception) to December 31, 2005, and the balance sheet data as of December 31, 2004 and 2005 from our audited financial statements, which are included in this prospectus. We have derived the consolidated statements of operations data for the years ended December 31, 2001 and 2002 and the consolidated balance sheet data as of December 31, 2001, 2002 and 2003 from our audited financial statements, which are not included in this prospectus. The cumulative statements of operations data for the period from March 31, 1998 (inception) through December 31, 2005 includes amounts for the period from March 31, 1998 (inception) to December 31, 2001, which were audited by auditors who have ceased operations. As described in note 2(o) to our financial statements included elsewhere in this prospectus, those financial statements have been restated. KPMG LLP, an independent registered public accounting firm, audited the adjustments described in note 2(o) that were applied to restate the cumulative financial statements for the period from March 31, 1998 (inception) to December 31, 2001. In KPMG's opinion, such adjustments are appropriate and have been properly applied. Our historical results for any prior period are not necessarily indicative of results to be expected for any future period.

	Year Ended December 31,					Period from March 31, 1998 (Inception) to December 31, 2005
	2001	2002	2003	2004	2005	
	(in thousands, except share and per share data)					
Statements of Operations Data:						
Revenues	$ —	$ 180	$ 756	$ 1,606	$ 4,967	$ 7,669
Operating expenses:						
Research and development	5,808	10,238	17,695	20,070	21,123	76,970
General and administrative	3,395	4,165	4,693	6,023	7,944	27,231
Total operating expenses	9,203	14,403	22,388	26,093	29,067	104,201
Loss from operations	(9,203)	(14,223)	(21,632)	(24,487)	(24,100)	(96,532)
Interest income	1,043	769	317	579	854	3,998
Interest expense	(54)	(270)	(358)	(184)	(141)	(1,007)
Loss before tax benefit	(8,214)	(13,724)	(21,673)	(24,092)	(23,387)	(93,541)
Tax benefit	—	232	235	451	479	1,397
Loss applicable to common stockholders	$ (8,214)	$ (13,492)	$ (21,438)	$ (23,641)	$ (22,908)	$ (92,144)
Basic and diluted loss per share applicable to common stockholders	$ (134,477)	$ (201,365)	$ (315,259)	$ (347,670)	$ (9,925)	
Shares used to compute basic and diluted loss per share applicable to common stockholders	62	67	68	68	2,308	
Pro forma basic and diluted net loss per common share (unaudited)					$ (2.11)	
Shares used to compute pro forma basic and diluted net loss per common share (unaudited)					10,831,634	

	As of December 31,				
	2001	2002	2003	2004	2005
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents and short-term investments	$ 32,507	$ 24,599	$ 41,570	$ 32,987	$ 37,840
Working capital	31,669	22,119	37,045	29,580	34,331
Total assets	44,401	34,800	49,054	38,968	43,974
Long-term debt, net of current portion	621	2,728	846	205	804
Deficit accumulated during the development stage	(10,666)	(24,157)	(45,595)	(69,237)	(92,144)
Total stockholders' equity	42,340	28,896	43,275	34,613	38,401

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this prospectus for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small-molecule drugs that target post-transcriptional control processes. Our current pipeline of clinical and preclinical product candidates addresses multiple indications, including genetic disorders, oncology and infectious diseases. Our three most advanced product development programs are:

- ***PTC124 for genetic disorders.*** We are currently conducting two Phase 2 clinical trials of PTC124 in patients with cystic fibrosis and one Phase 2 clinical trial of PTC124 in patients with Duchenne muscular dystrophy in cases in which a nonsense mutation is the cause of the disease. We have conducted an interim analysis of data from 15 patients who have completed their participation in our cystic fibrosis trials.
- ***PTC299 for oncology.*** In April 2006, we commenced a Phase 1a clinical trial of PTC299 in healthy volunteers in Belgium. If this Phase 1a trial is successful, we plan to initiate a Phase 1b clinical trial of PTC299 in late 2006 in patients with advanced solid tumors whose disease has progressed during therapy or for whom there is no effective therapy available.
- ***Hepatitis C development program.*** In March 2006, we entered into a collaboration with Schering-Plough Corporation for the development and commercialization of our compounds for the potential treatment of hepatitis C.

We are also conducting discovery programs focused on identifying new treatments for multiple therapeutic areas, including bacterial infections, anemia and musculoskeletal conditions.

We have generated significant losses as we have progressed our lead product candidates into clinical development and expect to continue to generate losses as we continue the clinical development of PTC124 and PTC299. Our net loss for 2005 was $22.9 million. As of December 31, 2005, we had a deficit accumulated during the development stage of $92.1 million.

Financial Operations Overview

Revenues

To date, we have not generated any product sale revenues. We have funded our operations primarily through the sale of equity securities, capital lease and equipment financings, foundation and government grants and collaboration revenues. Our revenues for 2005 were approximately $5.0 million, consisting primarily of grant revenues.

We have received grant funding from a variety of foundations and government agencies, including Cystic Fibrosis Foundation Therapeutics, Inc., the Muscular Dystrophy Association, Parent Project Muscular Dystrophy and the National Institutes of Health. Grants are awarded on a project basis. We recognize grant revenues as we receive funding or when preclinical, clinical or regulatory milestones are met.

In March 2006, we entered into a collaboration and license agreement with a subsidiary of Schering-Plough Corporation under which we and Schering-Plough are collaborating in the discovery, development and

commercialization of compounds for the treatment of HCV and other viral diseases. Pursuant to the collaboration agreement, Schering-Plough paid us an upfront non-refundable payment of $12.0 million. Our agreement with Schering-Plough provides for a research collaboration, in connection with which Schering-Plough has agreed to provide us with funding, based on a full-time equivalent rate, for an agreed upon number of full-time equivalent scientific or research and development personnel that we dedicate to the research program. The initial research term is three years. Schering-Plough has two options to extend the research term for an additional term of one year per option. Schering-Plough can terminate the research term in specified circumstances. Schering-Plough is responsible for worldwide clinical development and commercialization of any compounds that it elects to advance from our research collaboration. We are eligible to receive more than $200 million in payments if we achieve specified development, regulatory and sales milestones. We are also entitled to royalties on sales of products developed pursuant to the collaboration, with the royalty percentage based on specified thresholds of worldwide net product sales.

In December 2005, we entered into a research collaboration and exclusive option agreement with Bausch & Lomb under which Bausch & Lomb is evaluating compounds in our anti-angiogenesis program for the purpose of identifying potential candidates for development by Bausch & Lomb for the treatment of ophthalmic diseases associated with angiogenesis, including macular degeneration. Under the terms of the agreement, we granted Bausch & Lomb exclusive options to license selected compounds. Bausch & Lomb has one year from the date of the agreement to exercise any such option. In exchange for the one-year options, Bausch & Lomb paid us an upfront non-refundable option grant fee of $300,000 and agreed to provide us with research funding during the option term to compensate us for completing agreed research. Bausch & Lomb has the right to extend the option term with respect to certain specified compounds for an additional six months in exchange for an extension fee. As of December 31, 2005, we had recognized $50,000 of revenue pursuant to the agreement.

Research and Development Expense

Research and development expenses consist of the costs associated with our research activities, as well as the costs associated with our drug discovery efforts, conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings. Our research and development expenses consist of:

- external research and development expenses incurred under agreements with third-party contract research organizations and investigative sites, third-party manufacturing organizations and consultants;
- employee-related expenses, which include salaries and benefits for the personnel involved in our drug discovery and development activities; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We use our employee and infrastructure resources across multiple research projects, including our drug development programs. We track expenses related to our clinical programs on a per project basis. Accordingly, we allocate internal employee-related and infrastructure costs, as well as third-party costs, to each clinical program. We do not allocate expenses related to preclinical programs.

The following table summarizes our principal product development programs, including the related stages of development for each product candidate in development and the research and development expenses allocated to each clinical product candidate. The information in the column labeled "Estimated Completion of Current Trial" is our estimate of the timing of completion of the current clinical trial or trials for the particular product candidate. The actual timing of completion could differ materially from the estimates provided in the table.

Product Candidate	Indication	Phase of Development	Estimated Completion of Current Trial	Research and Development Expenses Year Ended December 31, 2003	2004	2005
					(in thousands)	
Clinical development:						
PTC124	Cystic Fibrosis; Duchenne Muscular Dystrophy	Phase 2	2006	$ 2,642	$ 6,018	$ 5,132
PTC299	Cancer	Phase 1a	2006	—	83	2,021
Total clinical development				2,642	6,101	7,153
Research and preclinical				15,053	13,969	13,970
Total research and development				$17,695	$20,070	$21,123

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of, or the period, if any, in which material net cash inflows may commence from, PTC124, PTC299 or any of our preclinical product candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our clinical trials and other research and development activities;
- the potential benefits of our product candidates over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates that we are developing or may develop in the future;
- future clinical trial results;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or other regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expense

General and administrative expense consists primarily of salaries and other related costs for personnel, including stock-based compensation expenses, in our executive, legal, business development, finance, accounting information technology and human resource functions. Other general and administrative expenses include facility-related costs not otherwise included in research and development expense; advertising and

promotional expenses; costs associated with industry and trade shows; and professional fees for legal services, including patent-related expenses, and accounting services.

We expect that general and administrative expense will increase in 2006 and in future periods as a result of increased payroll, expanded infrastructure, increased consulting, legal, accounting and investor relations expenses associated with being a public company and costs incurred to seek collaborations with respect to any of our product candidates.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash and cash equivalents and short-term investments. Interest expense consists of interest incurred to finance equipment, office furniture and fixtures.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our financial statements appearing at the end of this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

We recognize grant revenues as we receive the funding or when preclinical, clinical or regulatory milestones are met. Grant revenues are not refundable.

As described above, our collaboration agreements contain multiple elements, including non-refundable up-front license fees, research payments for ongoing research and development, payments associated with achieving development and regulatory milestones and royalties to be paid based on specified percentages of net product sales, if any. We consider a variety of factors in determining the appropriate method of revenue recognition under these arrangements, such as whether the elements are separable, whether there are determinable fair values and whether there is a unique earnings process associated with a particular element of an agreement.

We recognize revenue from non-refundable, up-front fees ratably over the term of our performance under the agreements. These payments are recorded as deferred revenue pending recognition. We recognize revenue related to research payments for ongoing research and development as the services are performed. Generally, the payments received are not refundable and are based on contractual cost per full-time equivalent employee working on the project. We have not yet received any payments associated with achieving development and regulatory milestones, nor have we yet received royalties on net product sales.

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued

expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. Examples of estimated accrued expenses include:

- fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- professional service fees.

Stock-Based Compensation

Through December 31, 2005, in accordance with Statement of Financial Accounting Standards, or SFAS, No. 123, *Accounting for Stock-Based Compensation*, we elected to account for stock-based employee compensation using the intrinsic-value method under Accounting Principles Board, or APB, Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations. As such, we did not record expense on employee stock options granted when the exercise price of the options was equal to the fair value of the underlying stock on the date of the grant. Pro forma information regarding net loss and loss per share is required by SFAS No. 123 and has been determined as if we had accounted for employee stock option grants under the fair value method prescribed by that statement. Information with regard to the number of options granted, market price of the grants, vesting requirements and the maximum term of the options granted appears in Note 2 to our financial statements. Stock-based payments to non-employees are measured at the fair value of the stock-based instruments issued or the fair value of the goods or services received, whichever is more readily determinable.

For stock-based payments to both employees and non-employees, the fair value of the stock is a significant factor in determining credits or charges to operations. Because, prior to this offering, our shares have not been publicly traded, we must estimate the fair value of our common stock. There is no certainty that the results of our estimation would be the value at which the shares would be traded for cash. Factors that we consider in determining the fair value of our common stock include:

- pricing of private sales of our preferred stock;
- prior valuations of stock grants and preferred stock sales and the effect of events, including the progression of our product candidates, that have occurred between the time of the grants or sales;
- comparative rights and preferences of the security being granted compared to the rights and preferences of our other outstanding equity;
- comparative values of public companies discounted for the risk and limited liquidity provided for in the shares we are issuing;
- perspective provided by unrelated valuation specialists;
- perspective provided by investment banks, including the likelihood of an initial public offering and our potential value in an initial public offering; and
- general economic trends.

Our board of directors has historically determined the fair value of our equity instruments, excluding preferred stock, based upon information available to it on the measurement dates. In connection with our grant of stock options in February 2005 and in February 2006, we performed a concurrent analysis to determine the fair market value of our common stock. We performed our analysis in accordance with applicable elements of the practice aid issued by the American Institute of Certified Public Accountants entitled *Valuation of Privately Held Company Equity Securities Issued as Compensation*. We used two primary valuation methodologies within the income approach to determine our enterprise valuation. First, we used a probability-weighted income approach that reduced our estimated cash flows based on the probability of successfully completing clinical trials. Second, we employed a traditional income approach that analyzed our manage-

ment's internal operating forecast without directly adjusting cash flows for the probability of success. We then weighted the probability-weighted income approach and the traditional income approach equally to arrive at a single enterprise value. Finally, we used that enterprise value in an option-pricing model to calculate the value of our outstanding common stock.

In December 2004, the Financial Accounting Standards Board, or FASB, issued SFAS No. 123(R), *Share-Based Payment*. SFAS No. 123(R) supersedes SFAS No. 123, APB Opinion No. 25 and its related implementation guidance. SFAS No. 123(R) will require compensation costs related to share-based payment transactions to be recognized in our financial statements. We will measure the amount of compensation cost based on the grant-date fair value of the equity or liability instruments issued. We will recognize compensation cost over the period that an employee provides service in exchange for the award. SFAS No. 123(R) is effective as of the beginning of the first interim or annual reporting period that begins after December 15, 2005. We cannot predict the full impact of adoption of SFAS No. 123(R) because it will depend on levels of share-based payments that we grant in the future. We have not yet determined the impact that implementing SFAS No. 123(R) will have on our results of operations or financial condition.

Income Taxes

As part of the process of preparing our financial statements, we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves estimating our actual current tax exposure together with assessing temporary differences resulting from differing treatments of items for tax and accounting purposes. These differences result in deferred tax assets and liabilities. As of December 31, 2005, we had federal net operating loss carryforwards of $52.5 million, which expire starting in 2018, and federal research and development credit carryforwards of $3.7 million. We also had state net operating loss carryforwards of $49.7 million, which expire starting in 2009, and state research and development credit carryforwards of $2.8 million. At December 31, 2005, we recorded a full valuation allowance against our net deferred tax asset of approximately $45.5 million, as our management believes it cannot at this time conclude that it is more likely than not they will be realized. If we determine in the future that we will be able to realize all or a portion of our net deferred tax asset, an adjustment to the deferred tax valuation allowance would increase net income in the period in which we make such a determination. The Tax Reform Act of 1986 contains provisions that may limit the utilization of net operating loss credit carryforwards available to be used in any given year in the event of a change in ownership.

Results of Operations

Year Ended December 31, 2005 Compared to Year Ended December 31, 2004

Revenues. Revenues were $5.0 million in 2005, an increase of $3.4 million from revenues of $1.6 million in 2004. The increase resulted primarily from a significant increase in the number of grants and the dollar value of the grants that we received in 2005. In particular, in 2005 we received grants totaling $2.7 million from two patient advocacy groups, Cystic Fibrosis Foundation Therapeutics, Inc. and the Muscular Dystrophy Association, related to the clinical development of PTC124. We continue to seek additional grant revenue opportunities.

Research and Development Expense. Research and development expense was $21.1 million in 2005, an increase of $1.0 million, or 5.2%, from $20.1 million in 2004. The increase resulted primarily from the following changes in costs:

- increased costs for preclinical studies and manufacturing for PTC299 of $1.6 million;
- increased costs for preclinical studies for PTC124 of $895,000; and
- decreased costs for clinical studies and manufacturing for PTC124 of $1.6 million.

We expect that research and development expenses will increase in the future as a result of increased manufacturing and clinical development costs primarily relating to our PTC124 and PTC299 clinical development programs. The timing and amount of these expenses will depend upon the outcome of our

ongoing clinical trials, particularly the costs associated with our ongoing Phase 2 clinical trials of PTC124 and our Phase 1a and planned Phase 1b clinical trials of PTC299. The timing and amount of these expenses will also depend on the costs associated with potential future clinical trials of our product candidates and the related expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs and product candidate manufacturing costs.

General and Administrative Expense. General and administrative expense was $7.9 million in 2005, an increase of $1.9 million, or 31.9%, from $6.0 million in 2004. The increase resulted principally from the following:

- increased personnel costs of $1.1 million attributable to increased salaries as well as increased headcount in legal and human resources;
- increased consulting expense of $290,000 related to commercialization planning and information technology infrastructure; and
- increased patent-related expense of $528,000 related to filings for PTC124, PTC299 and compounds in our HCV program.

We expect that general and administrative expense will increase in 2006 and in future periods as a result of increased payroll, expanded infrastructure, increased consulting, legal, accounting and investor relations expenses associated with being a public company, costs incurred to seek collaborations with respect to any of our product candidates and the stock-based compensation expense that we expect to record under SFAS No. 123(R).

Interest Income and Interest Expense. Interest income was $854,000 in 2005, compared to $579,000 in 2004. Interest expense was $141,000 in 2005, compared to $184,000 in 2004. The increase in interest income resulted from higher average interest rates in 2005, partially offset by lower average cash and cash equivalents and short-term investment balances during the year. The reduction in interest expense resulted from a reduction in our equipment financing and capital lease obligations during 2005.

Tax Benefit. We recognize tax benefits related to our sale of net operating losses in the New Jersey Tax Transfer Program. Our tax benefit was $479,000 in 2005 and $451,000 in 2004.

Year Ended December 31, 2004 Compared to Year Ended December 31, 2003

Revenues. Revenues were $1.6 million in 2004 and $756,000 in 2003. The increase resulted from an increase in the number of grants that we received in 2004.

Research and Development Expense. Research and development expense was $20.1 million in 2004, an increase of $2.4 million, or 13.4%, from $17.7 million in 2003. The increase resulted principally from the following:

- increased costs of clinical studies and manufacturing for PTC124 of $2.6 million;
- increased laboratory supply and library compound costs of $408,000;
- increased personnel costs of $1.1 million; and
- decreased in-process research and development of $1.4 million.

General and Administrative Expense. General and administrative expense was $6.0 million in 2004, an increase of $1.3 million, or 28.3%, from $4.7 million in 2003. The increase resulted principally from the following:

- increased personnel costs of $450,000 attributable to increased salaries and increased headcount in investor relations and general management;
- increased consulting expense of $419,000 related to increased legal and human resource temporary staffing;

- increased patent and legal expense of $254,000 related to filings for PTC124 and general corporate legal expenses; and
- increased miscellaneous corporate expenses of $216,000.

Interest Income and Interest Expense. Interest income was $579,000 in 2004, compared to $317,000 in 2003. Interest expense was $184,000 in 2004, compared to $358,000 in 2003. The increase in interest income resulted from higher average interest rates in 2004 and higher average cash and cash equivalents and short-term investment balances during the year. The reduction in interest expense resulted from a reduction in our equipment financing and capital lease obligations during 2004.

Tax Benefit. Our tax benefit related to our sale of net operating losses in the New Jersey Tax Transfer Program was $451,000 in 2004 and $235,000 in 2003.

Liquidity and Capital Resources

Sources of Liquidity

As a result of our significant research and development expenditures and the lack of any approved products to generate product sales revenue, we have not been profitable and have generated operating losses since we were incorporated in 1998. As such, we have funded our research and development operations primarily through sales of our preferred stock. Through December 31, 2005, we had received aggregate net proceeds of $128.5 million from these sales. We have also received funding from grant and foundation support, capital lease financings and interest earned on investments.

As of December 31, 2005, we had cash and cash equivalents and short-term investments of $37.8 million. We hold our cash and investment balances in a variety of interest-bearing instruments, including obligations of U.S. government agencies and money market accounts. We invest cash in excess of our immediate requirements with regard to liquidity and capital preservation. Wherever possible, we seek to minimize the potential effects of concentration and degrees of risk.

Cash Flows

The following table provides information regarding our cash flows and our capital expenditures for the years ended December 31, 2003, 2004 and 2005.

	Year Ended December 31,		
	2003	2004	2005
	(in thousands)		
Cash provided by (used in):			
Operating activities	$ (16,225)	$ (22,408)	$ (20,720)
Investing activities	13,618	(20,218)	(1,647)
Financing activities	32,223	13,425	26,555
Capital expenditures (included in investing activities above)	667	1,121	963

Net cash used in operating activities was $20.7 million for the year ended December 31, 2005, $22.4 million for the year ended December 31, 2004 and $16.2 million in the year ended December 31, 2003. The net cash used in each of these periods primarily reflects the net loss for those periods, offset in part by depreciation, and changes in operating assets and liabilities.

Net cash used in investing activities was $1.6 million for the year ended December 31, 2005 and $20.2 million for the year ended December 31, 2004. Net cash provided by investing activities was $13.6 million for the year ended December 31, 2003. Cash used in investing activities was primarily related to net purchases of investments, and to a lesser extent, purchases of property and equipment.

Net cash provided by financing activities was $26.6 million for the year ended December 31, 2005, $13.4 million for the year ended December 31, 2004 and $32.2 million for the year ended December 31, 2003. Net cash provided by financing activities in 2005 was primarily attributable to the $26.5 million in proceeds

that we received from our Series E-2 preferred stock financing, and to a lesser extent, proceeds of $1.4 million in debt financing used to acquire property and equipment. Partially offsetting these proceeds were payments on debt obligations of $1.2 million. Net cash provided by financing activities in 2004 was primarily attributable to the subsequent closings on our Series E preferred stock financing, which initially closed in December 2003, totaling $14.9 million. Partially offsetting these proceeds were payments on debt obligations of $1.9 million. Net cash provided by financing activities in 2003 was primarily attributable to the initial closing of our Series E preferred stock financing totaling $34.2 million. Partially offsetting these proceeds were payments on debt obligations of $2.0 million.

Funding Requirements

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments and research funding that we expect to receive under our collaborations, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements until . We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we enter into collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials. Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical trials of PTC124 and PTC299;
- the success of our hepatitis C virus collaboration with Schering-Plough;
- the scope, progress, results and costs of preclinical development and laboratory testing and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the extent to which we acquire or invest in businesses, products and technologies; and
- our ability to establish and maintain collaborations.

We do not anticipate that we will generate product revenue for at least the next several years. In the absence of additional funding, we expect our continuing operating losses to result in increases in our cash used in operations over the next several quarters and years. To the extent our capital resources are insufficient to meet our future capital requirements, we will need to finance our future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. Except for research funding by our collaborators, particularly Schering-Plough, we do not currently have any commitments for future external funding.

Additional equity or debt financing, grants, or corporate collaboration and licensing arrangements, may not be available on acceptable terms, if at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain drug candidates that we might otherwise seek to develop or commercialize independently. In addition, any future equity funding may dilute the ownership of our equity investors.

Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2005 (in thousands).

	Total	Less than 1 Year	1-3 Years	4-5 Years	More than 5 Years
Equipment financing obligations	$ 1,282	$ 478	$ 774	$ 30	—
Operating lease obligations	1,338	384	785	169	—
Total fixed contractual obligations	$ 2,620	$ 862	$ 1,559	$ 199	—

Quantitative and Qualitative Disclosures About Market Risk

The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and investments in a variety of securities of high credit quality. As of December 31, 2005, we had cash and cash equivalents and short-term investments of $37.8 million. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our investments are short-term in duration, we believe that our exposure to interest rate risk is not significant and a 1% movement in market interest rates would not have a significant impact on the total value of our portfolio. We actively monitor changes in interest rates.

Recent Accounting Pronouncements

In December 2004, the FASB issued SFAS No. 123(R). SFAS No. 123(R) supersedes SFAS No. 123, APB Opinion No. 25 and its related implementation guidance. SFAS No. 123(R) will require compensation costs related to share-based payment transactions to be recognized in the financial statements. The amount of compensation cost will be measured based on the grant-date fair value of the equity or liability instruments issued. Compensation cost will be recognized over the period that an employee provides service in exchange for the award. SFAS No. 123(R) is effective as of the beginning of the first interim or annual reporting period that begins after December 15, 2005. We cannot predict the full impact of adoption of SFAS No. 123(R) at this time because it will depend on levels of share-based payments granted in the future. We have not yet determined the impact that implementing SFAS No. 123(R) will have on our results of operations or financial condition.

In June 2005, the FASB issued SFAS No. 154, *Accounting Changes and Error Corrections*. This statement requires that a voluntary change in accounting principle be applied retrospectively with all prior period financial statements presented on the basis of the new accounting principle, unless it is impracticable to do so. SFAS No. 154 also provides that (1) a change in method of depreciating or amortizing a long-lived nonfinancial asset be accounted for as a change in estimate (prospectively) that was effected by a change in accounting principle, and (2) correction of errors in previously issued financial statements should be termed a “restatement.” The new standard is effective for accounting changes and correction of errors made in fiscal years beginning after December 15, 2005. Early adoption of this standard is permitted for accounting changes and correction of errors made in fiscal years beginning after June 1, 2005. We do not anticipate that the adoption of this statement will have a material impact on our results of operations or financial condition.

In November 2005, the FASB issued FASB Staff Position FAS 115-1 and FAS 124-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*. This Staff Position addresses the determination as to when an investment is considered impaired, whether that impairment is other than temporary and the measurement of an impairment loss. This Staff Position also includes accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. The guidance in the Staff Position is required to be applied to reporting periods beginning after December 15, 2005. We will adopt the provisions of this Staff Position in 2006 and do not currently believe that implementation will have a material effect on our results of operations or financial condition.

BUSINESS

Overview

We are a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small-molecule drugs that target post-transcriptional control processes. Our lead product development programs are PTC124 for genetic disorders and PTC299 for oncology. We have discovered all of our compounds currently under development. We plan to develop these compounds both on our own and through selective collaboration arrangements with leading pharmaceutical and biotechnology companies. We have retained worldwide commercialization rights to PTC124 and PTC299 and recently entered into a collaboration with Schering-Plough Corporation for the development and commercialization of preclinical compounds that we have identified for the potential treatment of hepatitis C.

Post-transcriptional control processes regulate the rate and timing of protein production and are of central importance to proper cellular function. The small-molecule compounds that we are developing are designed to alter post-transcriptional processes and modulate the utilization of messenger RNA, or mRNA, a key intermediate in protein production. We have assembled proprietary technologies and extensive knowledge of post-transcriptional control processes that we apply in our drug discovery and development activities. We believe that systematically targeting these processes represents a new and unexploited approach to drug discovery and development, which has several potential key advantages. These include the potential to use orally available small-molecule drugs to address previously intractable drug targets and to up or down regulate the level of production of a protein of interest. In addition, this approach has the potential to treat a broad range of diseases. Our current pipeline of clinical and preclinical product candidates addresses multiple indications, including genetic disorders, oncology and infectious diseases.

Our three most advanced product development programs are:

- ***PTC124 for genetic disorders.*** We are developing PTC124 for the treatment of patients with genetic disorders that arise as a result of a type of genetic mutation known as a nonsense mutation. Our initial target indications for PTC124 are cystic fibrosis and Duchenne muscular dystrophy in cases in which a nonsense mutation is the cause of the disease. We are currently conducting two Phase 2 clinical trials of PTC124 in patients with cystic fibrosis and one Phase 2 clinical trial of PTC124 in patients with Duchenne muscular dystrophy. We recently performed an interim analysis of data from 15 patients who have completed our ongoing cystic fibrosis trials and observed results which suggest that PTC124 may have pharmacological activity that addresses the underlying cause of cystic fibrosis in these patients.
- ***PTC299 for oncology.*** We are developing PTC299 initially for the treatment of cancer. In April 2006, we commenced a Phase 1a clinical trial of PTC299 in healthy volunteers in Belgium. If this Phase 1a clinical trial is successful, we plan to initiate a Phase 1b clinical trial of PTC299 in cancer patients in late 2006.
- ***Hepatitis C development program.*** We have identified a number of small-molecule compounds that, in preclinical tests, inhibited hepatitis C viral protein synthesis and the production of the virus. These compounds target a specific site on the viral mRNA known as an internal ribosomal entry site, or IRES, which is critical to the replication of the hepatitis C virus. In March 2006, we entered into a collaboration with Schering- Plough for the development of these compounds.

We are also conducting discovery programs focused on developing new treatments for multiple therapeutic areas, including bacterial infections, anemia and musculoskeletal conditions.

The PTC Approach

Our approach to drug discovery and development is to systematically target post-transcriptional control processes that can be modulated by small-molecule therapeutics. We believe this may provide several potential advantages in comparison with conventional approaches to drug discovery and development. The following are some of the key potential advantages of our approach.

Unexploited area of drug discovery and development. Targeting post-transcriptional control processes is a new field for drug discovery. We believe that focusing on post-transcriptional control processes will enable us both to address known drug targets through new mechanisms of action and to pursue a broad range of targets that have previously not been amenable to drug discovery. Our approach is a complex endeavor that requires a comprehensive understanding of post-transcriptional control processes and the development of specialized secondary functional assays to characterize the interaction between a drug candidate and a target of interest. We believe that a large number of promising post-transcriptional control drug targets remain unexploited, providing a significant opportunity for our integrated and systematic approach to drug discovery.

Broad applicability to address intractable drug targets and unmet medical needs. One common approach to drug discovery is to use high-throughput screening assays to identify compounds that inhibit enzymatic activity. However, this approach often does not permit the identification of compounds that enhance enzymatic activity. In addition, this drug discovery approach does not work for the large number of medically relevant drug targets whose function is unknown or that are not amenable to traditional screening. In contrast, drugs that interact with components of the post-transcriptional control apparatus can effectively act as therapeutics by either increasing the production of a needed protein or by reducing the production of an undesirable protein. We also believe that drugs can be designed to regulate the production of a specific protein without otherwise interfering with normal operation of the cell. Because post-transcriptional control is important to the modulation of the amounts of many types of proteins, we believe that these types of therapeutics may have the potential to treat a wide variety of diseases for which there is an unmet medical need, including genetic disorders, cancer, anemia and musculoskeletal disorders, as well as inflammation, metabolic disorders, cardiovascular conditions and neurological disorders. Targeting post-transcriptional control processes may also be applicable to treating infectious diseases, including viral infections, in which the virus acts by harnessing the infected body's post-transcriptional control processes and bacterial infections, in which the bacteria have their own distinct post-transcriptional control processes.

Use of small molecules. Our focus is on developing orally available small molecules. In contrast, many of the alternative therapies that can overcome some of the limitations of traditional small-molecule drug screening approaches, such as biologics, antisense, gene therapy and RNAi, are generally unable to be delivered orally. As a result, problems with effective treatment delivery have hampered development of many of these newer experimental approaches. Our small molecules have the potential to replace these expensive and difficult to administer therapeutics with pills, tablets or orally administered liquids, which are generally more convenient and may enhance patient compliance. We also expect to be able to take advantage of the general ease of synthesis of small-molecule production and the extensive pharmaceutical industry experience with manufacturing, formulating and distributing small-molecule drugs.

Proof of concept. There are several marketed drugs that act by affecting post-transcriptional control processes. These drugs include the aminoglycoside antibiotics, such as gentamicin, other antibiotics, including erythromycin and linezolid, and some immunosuppressant drugs, such as rapamycin. Although the majority of these drugs were developed without prior knowledge of their mechanism of action, we believe that what is now known about the manner in which they act validates the potential of our approach. Accordingly, we believe that a methodical and scientific approach to the identification and selection of drugs that target post-transcriptional control processes has significant commercial potential.

Our Product Development Programs

The following table summarizes key information about our product candidates that are in clinical trials and our other principal product development and discovery stage programs. All of the compounds in these programs are new chemical entities identified using our technologies and developed through our own internal research efforts.

Program	Development Status	Commercialization Rights
PTC124 for genetic disorders	Phase 2 clinical trials in cystic fibrosis and Duchenne muscular dystrophy ongoing; analysis of interim data from cystic fibrosis trials completed	PTC
PTC299 for oncology	Phase 1a clinical trial in healthy volunteers ongoing; Phase 1b clinical trial in cancer patients planned	PTC
Hepatitis C virus program	Preclinical	Schering-Plough Corporation
Antibacterial program	Discovery	PTC
Anemia program	Discovery	PTC
Musculoskeletal program	Discovery	PTC
Ophthalmology program	Subject of research collaboration	Bausch & Lomb

PTC124

PTC124 is a novel, orally administered small-molecule compound that targets a particular genetic alteration known as a nonsense mutation. We are developing PTC124 for the treatment of genetic disorders in which a nonsense mutation is the cause of the disease because we believe that PTC124 may restore the protein functionality that is lost as a result of the mutation. In the fourth quarter of 2005, we commenced two Phase 2 clinical trials of PTC124 for cystic fibrosis caused by nonsense mutations and one Phase 2 clinical trial of PTC124 for Duchenne muscular dystrophy caused by nonsense mutations. We have conducted an interim analysis of data from a total of 15 patients who have completed their participation in our cystic fibrosis trials. We believe that our findings to date support our continued development of PTC124 both in cystic fibrosis and in other genetic disorders caused by nonsense mutations. We expect to complete our ongoing Phase 2 clinical trials of PTC124 in the second half of 2006.

The FDA has granted fast track designation and orphan drug designation to PTC124 for the treatment of both cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations. The European Medicines Agency, or EMEA, has granted orphan drug status to PTC124 for the treatment of both cystic fibrosis and Duchenne muscular dystrophy.

Background on Genetic Disorders and Nonsense Mutations

The National Institutes of Health Office of Rare Diseases estimates that rare disorders afflict 25 million people in the United States. Based on our research, we estimate that there are at least 1,800 distinct genetic disorders, including cystic fibrosis, Duchenne muscular dystrophy, spinal muscular atrophy, hemophilia, lysosomal storage disorders, retinitis pigmentosa, familial hypercholesterolemia and some forms of cancer. We also estimate that, on average, 5% to 15% of patients with any genetic disorder have a nonsense mutation as the cause of the disease. Because genetic disorders are often a consequence of the absence of a single protein, the restoration of the production of that protein has the potential to treat the genetic disorder.

Through the post-transcriptional process of translation, a specialized cellular apparatus, called the ribosome, builds functional proteins by translating the genetic code contained in the mRNA. This decoding process reads the building blocks of the mRNA, known as nucleotides, in groups of three. Each group of three

nucleotides is called a codon. Three of the 64 possible codons contained in mRNA serve as normal stop signals and indicate the end of the protein-coding region of the mRNA. When functioning properly, the stop codons cause the ribosome to halt translation of the mRNA once the mRNA's genetic code has been completely translated into a full-length, functional protein.

There are four basic types of mutations in DNA that can cause a genetic disorder. These are known as insertion, deletion, missense and nonsense mutations. A nonsense mutation is a single nucleotide alteration in the DNA that, when copied to mRNA, is interpreted by the ribosome as a premature stop signal in the protein-coding region of the mRNA. As a result, the translation process is halted before a full-length, functional protein is formed. The resulting truncated protein is too short to serve its necessary function, and the absence of a full-length, functional protein may cause disease.

Cystic Fibrosis

Cystic fibrosis is among the most common life-threatening genetic disorders worldwide. According to the Cystic Fibrosis Foundation, the disease affects approximately 30,000 adults and children in the United States and, according to the European Cystic Fibrosis Foundation, it affects a similar number of patients in Europe. Cystic fibrosis occurs in approximately one of every 3,500 live births, with approximately 1,000 new cases diagnosed each year in the United States. There is a commercially available genetic test to determine if a patient's cystic fibrosis is caused by a nonsense mutation. The Cystic Fibrosis Foundation estimates that approximately 83% of the active patients in their National Patient Registry have been genotyped. Based on information provided to us by the Cystic Fibrosis Foundation, we estimate that nonsense mutations are the cause of cystic fibrosis in approximately 10% of patients in the United States.

Cystic fibrosis is caused by defects in a single gene known as the cystic fibrosis transmembrane conductance regulator, or CFTR. The CFTR gene encodes the CFTR protein, which is used by the body to transport chloride across cell membranes. Genetic mutations that result in the loss of function of the CFTR protein cause the body to produce abnormally thick and sticky mucus that clogs the lungs, obstructs the pancreas and blocks the bile duct in the liver. This leads to life-threatening lung infections, permanent pancreatic damage and malnutrition because digestive enzymes from the pancreas do not reach the intestines to help break down and absorb food. Because patients with cystic fibrosis have malabsorption and a high calorie expenditure for breathing, their body weights can often be low.

Complications from lung infections are the primary cause of death from cystic fibrosis. From as early as four months of age, patients with cystic fibrosis may begin to develop airway obstruction and inflammation. Over time, most patients develop chronic bacterial infections in the airways, resulting in repeated episodes of pneumonia. Ultimately, progressive lung dysfunction leads to respiratory failure and death. According to the Cystic Fibrosis Foundation's National Patient Registry, the median age of survival for a person with cystic fibrosis is in the mid-30s.

There is currently no available therapy to correct defective CFTR production and function. Instead, available treatments for cystic fibrosis are designed to alleviate the symptoms of the disease. These treatments include chest physical therapy to clear the thick mucus from the lungs, antibiotics to treat lung infections and a mucus-thinning drug designed to reduce the number of lung infections and improve lung function. In addition, the majority of cystic fibrosis patients take pancreatic enzyme supplements to assist with food absorption in digestion.

There is a significant unmet medical need for a treatment for the underlying cause of cystic fibrosis. We believe that PTC124 may be a suitable treatment for the subset of cystic fibrosis patients whose disease is caused by a nonsense mutation.

Duchenne Muscular Dystrophy

Muscular dystrophies are genetic disorders characterized by progressive muscle wasting and weakness. There are several types of muscular dystrophy, of which Duchenne muscular dystrophy is the most common and one of the most severe. Duchenne muscular dystrophy occurs when a mutation in the dystrophin gene

prevents the cell from making a functional dystrophin protein. Dystrophin is critical to the structural stability of the fibers in skeletal, diaphragm and heart muscle. The absence of normally functioning dystrophin results in muscle fragility and muscle injury when muscles are stretched during normal use. As muscle damage progresses, connective tissue and fat replace muscle fibers.

Because the dystrophin gene is located on the X chromosome, Duchenne muscular dystrophy occurs almost exclusively in young boys. According to Parent Project Muscular Dystrophy, Duchenne muscular dystrophy occurs in approximately 1 in 3,500 live male births, with approximately 20,000 new cases diagnosed each year worldwide. Based on this incidence data, we estimate that Duchenne muscular dystrophy affects approximately 12,000 boys and adolescents in the United States and a similar number of patients in Europe. As with cystic fibrosis, genetic tests are available to determine if a patient's Duchenne muscular dystrophy is caused by a nonsense mutation. Based on the testing records of the Utah Dystrophinopathy Project, we estimate that a nonsense mutation is the cause of Duchenne muscular dystrophy in approximately 13% of patients in the United States.

Children with Duchenne muscular dystrophy typically begin to show symptoms as early as age three, when they develop a waddling gait, may seem clumsy and often fall. Progressive weakness then develops in the voluntary muscles in the arms, legs and trunk. This muscle weakness results in fixations, known as contractures, of joints such as knees, hips, elbows and feet. By the age of eight, most subjects have difficulty ascending stairs. By the age of 10 to 12, many are confined to wheelchairs. By the early teens, patients' hearts and respiratory muscles are also often affected. The wheelchair dependence of a Duchenne muscular dystrophy patient results in further loss of strength and the weakening of heart and lung muscles. This eventually results in fatal heart or lung failure. The average age of survival of Duchenne muscular dystrophy patients is 20 to 25 years.

As with cystic fibrosis, there is currently no available therapy to improve or correct dystrophin production and function. As a result, currently available treatments for Duchenne muscular dystrophy are palliative in nature. These treatments seek to address the symptoms through supportive care measures, such as bracing to give patients some opportunity to remain standing, joint stretching exercises to avoid contractures, tendon release surgery and eventual wheelchair use and assisted ventilation. Corticosteroids are also often prescribed to treat and delay the onset of the symptoms of the disease but cause significant complications.

There is a significant unmet medical need for a treatment for the underlying cause of Duchenne muscular dystrophy. We believe that PTC124 may be a suitable treatment for the subset of Duchenne muscular dystrophy patients whose disease is caused by a nonsense mutation.

PTC124 Scientific Background

We believe that a drug with a mechanism of action that allows the ribosome to read through premature stop codons without affecting the normal termination of protein synthesis may be able to overcome the effects of nonsense mutations. For example, in *in vitro*, animal and human studies, the antibiotic gentamicin has demonstrated the ability to bind to ribosomes in a manner that causes the ribosomes to read through a premature stop signal and continue the translation process to produce a full-length, functional protein. Specifically, in animal studies in which gentamicin was administered at high doses, the study animals produced full-length versions of the CFTR and dystrophin proteins. In addition, in a study conducted in Israel on 19 patients with cystic fibrosis caused by a nonsense mutation, the administration of gentamicin as nose drops restored CFTR protein function in the membranes of the nasal mucosa cells of 90% of the patients. Although these results involving gentamicin serve as a proof of concept for the read through of nonsense mutations as a therapeutic approach to treating genetic disorders, we believe that gentamicin's serious dose-limiting toxicities and need for intravenous administration make it an unattractive treatment for these disorders.

PTC124 also allows the cellular machinery to read through premature stop codons in mRNA, and thereby enables the translation process to produce full-length, functional proteins. However, PTC124 is from a distinct structural class that we believe acts at a different location on the ribosome than gentamicin and does

not have antibiotic properties. We do not expect PTC124 to have the serious dose-limiting toxicities associated with gentamicin.

Preclinical Development of PTC124

We have conducted multiple *in vitro* and animal preclinical studies of PTC124. Key findings of these studies include the following:

- The administration of PTC124 resulted in the production of full-length and functionally active CFTR in a mouse model of cystic fibrosis. Similarly, the administration of PTC124 resulted in the production of full-length and functionally active dystrophin in both *in vitro* and animal models of Duchenne muscular dystrophy.
- PTC124 demonstrated greater potency and activity than gentamicin controls in the read through of premature stop codons in *in vitro* studies.
- In *in vitro* and animal safety pharmacology studies, PTC124's activity was specific for the premature stop codons resulting from nonsense mutations. There was no evidence of read through of normal stop codons in these studies, even when PTC124 was tested at significantly higher plasma concentrations than those that we expect to see in patients.

PTC124 demonstrated an acceptable toxicity profile when tested at high exposure levels in rats and dogs. In these studies, we did not observe any meaningful toxicity to vital organs, including brain, liver, kidneys, heart, lungs and ears. In our long-term toxicology study in dogs, we noted inflammatory cells in the adrenal glands of the dogs that were treated with PTC124. We did not observe a similar finding in rats. We are evaluating the functional consequences of this observation in the dogs. The clinical implications, if any, are unknown at this time. Some rats developed brown fat tumors at PTC124 levels that were significantly higher than those that we expect to observe in our clinical trials. Brown fat is functionally important in rats but has little importance in humans. Accordingly, tumors of brown fat are extremely rare in humans. Other drugs known to cause growth of brown fat tumors in rats have not been observed to cause similar tumors in humans. In addition, one female rat that received PTC124 and one female rat in the control group were noted to have nonmetastatic tumors of the mammary glands, and two male rats that received PTC124 had nonmetastatic tumors of the testes. Given the isolated occurrence and distribution of these non-brown fat tumors across the treatment groups, it was not clear whether the occurrence of these tumors in the rats was specifically caused by PTC124. We did not observe any tumors or pre-cancerous lesions in dogs. At the request of the FDA, we are conducting an additional six-month toxicity study of PTC124 in rats.

Clinical Development of PTC124

Phase 1 Clinical Trials. In our clinical trials, we are administering PTC124 orally as a liquid suspension comprising a powdered form of the compound mixed with water. We designed this formulation because PTC124 is being administered to children, who often have difficulty swallowing pills or capsules.

We have completed two Phase 1 clinical trials of PTC124 involving a total of 62 healthy volunteers. The first Phase 1 trial was a single-dose, randomized, placebo-controlled safety and pharmacokinetic study conducted in a total of 31 healthy volunteers between the ages of 18 and 30. In the first stage of the trial, subjects were enrolled at escalating dose levels ranging from 3 to 200 mg/kg. In this study, we determined that 100 mg/kg is the maximum tolerated dose based on the observation of increased frequency of headaches, dizziness and mild gastrointestinal events, such as nausea, vomiting and diarrhea, at the 150 mg/kg and 200 mg/kg doses. The drug was palatable, with no obvious odor or taste. In the second stage of this trial, we assessed the effect of food on the safety and pharmacokinetic profiles of PTC124 at a dose of 50 mg/kg. This study provided us with pharmacokinetic data that indicated minimal alterations in the pharmacokinetic profile when PTC124 was taken after a meal and supported giving PTC124 with food to maintain plasma concentrations. The study also provided pharmacokinetic information allowing us to predict PTC124 blood exposure levels in future studies.

The second Phase 1 trial was a multiple-dose, open-label safety and pharmacokinetic study conducted in a total of 31 healthy volunteers between the ages of 18 and 30. In the first stage of the trial, subjects were enrolled at escalating twice-daily doses ranging from 10 to 50 mg/kg per dose taken with food for seven consecutive days. In the second stage of this trial, subjects were enrolled at a twice-daily dose of 50 mg/kg per dose for 14 days. In this study, there were no clinically significant adverse events reported at any dose tested, although we observed modest elevations of liver enzymes in some subjects. These elevated enzyme levels did not require cessation of PTC124 administration, and enzyme levels typically normalized after completion of the treatment phase. We did not observe any increases in bilirubin, which can be associated with serious harm to the liver. As in the single-dose study, we were able to achieve and maintain plasma concentrations of PTC124 that, based on preclinical data, we believe may have a therapeutic effect. In the multiple-dose trial, as in the single-dose study, we sought to determine whether PTC124 promoted improper read through of normal stop codons. We assessed this by observing whether the trial participants produced improperly large forms of specified proteins. We did not observe any such improper protein formation.

Phase 2 Clinical Trials for Cystic Fibrosis. In the fourth quarter of 2005, we commenced two open-label Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis caused by nonsense mutations. In each trial, we expect to enroll at least 18 evaluable patients age 18 years or older who have been diagnosed with cystic fibrosis resulting from a nonsense mutation in the CFTR gene. The goals of these trials are to obtain indications of pharmacological activity and to assess dose response, safety and pharmacokinetics. We are conducting one trial at the Hadassah University Hospital in Jerusalem, Israel and the second trial at four sites in the United States. We are performing the trial in Israel because the incidence of cystic fibrosis caused by a nonsense mutation is significantly higher in Israel than elsewhere in the world and because the investigators at the Hadassah University Hospital have past experience in conducting similar types of studies. All U.S. sites are member institutions of the Cystic Fibrosis Therapeutics Development Network, a network of 18 cystic fibrosis care centers with extensive experience in conducting clinical trials.

The trial designs are comparable and include two treatment cycles. Each cycle consists of a two-week period of continuous PTC124 treatment, and then a two-week follow-up period without PTC124 treatment. During the two weeks of PTC124 treatment in the first cycle, participants receive a lower-dose regimen of PTC124, consisting of 4 mg/kg with breakfast, 4 mg/kg with lunch and 8 mg/kg with dinner, for a total daily dose of 16 mg/kg. During the two weeks of PTC124 treatment in the second cycle, the same participants receive a higher-dose regimen of PTC124, consisting of 10 mg/kg with breakfast, 10 mg/kg with lunch and 20 mg/kg with dinner, for a total daily dose of 40 mg/kg. We established these dosing regimens based on pharmacokinetic modeling from our Phase 1 clinical trials with the goal of achieving plasma concentrations of PTC124 that, based on our preclinical models, we anticipate may have a therapeutic effect. We evaluate trial participants at the beginning and end of each two-week treatment period and follow-up period in each cycle.

The objective in both trials is to determine the change in CFTR-mediated chloride conductance in respiratory cells as measured between the beginning and end of treatment for each study participant. To make this determination, we measure the patient's transepithelial potential difference, or TEPD. TEPD is assessed by means of a standardized, minimally invasive procedure. In the procedure, a small plastic catheter is used to assess electrical differences across the outer cell membrane of nasal mucosa cells in the nostril. TEPD values are expressed in millivolts, or mV. A chloride conductance equal to or more electrically negative than -5.0 mV is generally considered to be in the normal range. Because of the role of the CFTR protein in transporting chloride across cell membranes and because of the absence of this protein in cystic fibrosis patients, these patients have an abnormal TEPD chloride conductance. Cystic fibrosis patients with TEPD values closer to normal are more likely to have better lung function and are less likely to develop acute lung infections. As a result, TEPD serves as a marker for the diagnosis and prognosis of cystic fibrosis. TEPD has become the standard primary pharmacodynamic endpoint for Phase 1 and Phase 2 clinical trials for drugs aimed at correcting CFTR dysfunction.

Interim Data from Phase 2 Clinical Trials for Cystic Fibrosis. In March 2006, we conducted an interim analysis of data from a total of 15 patients who have completed their participation in the trials. We believe that our findings to date support our continued development of PTC124 both in cystic fibrosis and in other genetic disorders caused by nonsense mutations. The following discussion of the interim data from the trials combines

data from the 15 patients from both the U.S. and Israeli trials. These results have become recently available. New information may arise from our continuing analysis of the data that may be less favorable than the data presented below. The results from additional patients enrolled in the ongoing studies may cause the final results of our trials to differ from the data for the 15 patients presented below. In addition, we are conducting these trials as open-label studies, which are generally considered to be less conclusive than blinded studies.

Endpoints. The primary endpoint in both trials is the change in TEPD chloride conductance. We have assessed this endpoint by dose level in the following three ways:

- *Mean change in TEPD chloride conductance.* This is the average among all study participants of the changes from the beginning to the end of the treatment period in each participant's TEPD chloride conductance. For example, if the study consisted of three participants and if the changes in TEPD chloride conductance for the three participants were -7.0 mV, -2.0 mV and -9.0 mV, the mean change in TEPD chloride conductance among these participants would be -6.0 mV.
- *Percentage of patients with a chloride conductance response.* This is the percentage of patients who demonstrated a TEPD chloride conductance response at the end of each treatment period with PTC124. For purposes of the trials, a chloride conductance response is defined as a TEPD chloride conductance improvement of at least -5.0 mV. For example, in a patient with a TEPD chloride conductance value of +1.0 mV at baseline and a TEPD chloride conductance value of -6.0 mV at the end of treatment, the TEPD chloride conductance improvement would be -7.0 mV, representing a chloride conductance response.
- *Percentage of patients with improvements of TEPD chloride conductance values into the normal range.* As noted above, a chloride conductance equal to or more electrically negative than -5.0 mV is generally considered to be in the normal range. As such, a patient with a TEPD chloride conductance value of +1.0 mV at baseline would be considered to have an abnormal value because the value is more electrically positive than -5.0 mV. If, at the end of treatment, that patient's TEPD chloride conductance value improved to -6.0 mV, this would represent an improvement into the normal range because the improved value is more electrically negative than -5.0 mV.

Secondary endpoints include lung function testing, with measurements of forced expiratory volume in one second, or FEV_1, and forced vital capacity, or FVC; overall safety profile as evaluated by measuring the type, frequency, severity, timing and relationship to PTC124 of any adverse events, laboratory abnormalities or electrocardiogram abnormalities; study drug compliance as assessed by quantification of used and unused PTC124; and pharmacokinetics of PTC124 as evaluated by frequent blood sampling on the first day and last day of each treatment period. Although not predetermined endpoints in the trial protocols, we are also assessing changes in patients' body weights and patient-reported improvements, if any, in cystic fibrosis-related symptoms.

Inclusion and Exclusion Criteria. Key inclusion criteria for study participants include a diagnosis of cystic fibrosis caused by a nonsense mutation; an abnormal TEPD chloride conductance at baseline; age of at least 18 years; body weight of at least 40 kilograms and FEV_1 at baseline of at least 40% of normal, based on patient gender, age and height. Key exclusion criteria for study participants include ongoing acute illness, including acute upper or lower respiratory infections within two weeks prior to study treatment; history of major complications of lung disease within two months prior to start of study treatment; abnormal chest x-ray; substantial liver abnormalities; abnormalities of kidney function; and ongoing use of or changes in specified medications.

Patient Demographics. Of the 15 patients included in the interim analysis, three were from the U.S. trial and 12 were from the Israeli trial. Seven patients were male and eight were female. Patients had a median age of 22 years. Three of the most common types of nonsense mutations in the CFTR gene were represented among the 15 patients. All patients had multiple signs and symptoms of cystic fibrosis, including some degree of lung dysfunction. Based on patient gender, age and height, the mean FEV_1 value at study entry was 64% of normal and the mean FVC value at study entry was 79% of normal. Fourteen of the 15 patients included in the interim analysis had airway colonization with *Pseudomonas aeruginosa*, a common bacterial

infection in cystic fibrosis patients that can lead to serious pneumonia. Fourteen of the 15 patients also had pancreatic insufficiency and required chronic pancreatic enzyme replacement therapy. The patients included in the interim analysis had relatively low body weights, with a mean weight of 58.3 kilograms, or 128.5 pounds, at study entry.

TEPD Results. In the 15 patients included in the interim analysis, at both dose levels, we observed:

- statistically significant mean improvements in TEPD chloride conductance;
- statistically significant percentages of patients with a TEPD chloride conductance response; and
- statistically significant increases in the percentage of patients with a TEPD chloride conductance value in the normal range.

The statistical significance of clinical trial results is determined by statistical methods that establish the p-value of the results. Typically, clinical trial results are statistically significant if they have a p-value of 0.05 or less, meaning that there is less than a one-in-twenty likelihood that the observed results occurred by chance.

We believe that these results suggest that PTC124 has meaningful pharmacological activity that is consistent with our hypothesis that treatment with PTC124 can restore the production and function of CFTR protein in patients with cystic fibrosis caused by a nonsense mutation. We also believe that this is the first time such activity has been observed in a clinical trial of an oral therapy for cystic fibrosis.

The following table presents the TEPD results for the 15 patients included in the interim analysis. For each measurement, we present the results on a best-of-nostrils and mean-of-both-nostrils basis. Historically, results of TEPD tests have typically been presented on a best-of-nostrils basis. However, recent guidelines established by the Cystic Fibrosis Therapeutics Development Network recommend that TEPD results be presented on both bases.

	Lower Dose Level		Higher Dose Level	
TEPD Result	**Result**	**p-Value**	**Result**	**p-Value**
Mean change in TEPD chloride conductance:				
Best of nostrils	-9.0 mV	<0.001	-6.4 mV	0.009
Mean of both nostrils	-6.7 mV	<0.001	-4.4 mV	0.023
Number of patients with[3] -5 mV improvement in TEPD chloride conductance:				
Best of nostrils	9/15 (60)%	<0.001	8/15 (53)%	<0.001
Mean of both nostrils	6/15 (40)%	0.005	7/15 (47)%	<0.001
Number of patients with improvement in TEPD chloride conductance to normal:				
Best of nostrils	8/15 (53)%	0.008	8/15 (53)%	0.008
Mean of both nostrils	6/15 (40)%	0.032	7/15 (47)%	0.016

The treatment effects at the lower and higher dose levels of PTC124 were not statistically significantly different. In addition, we observed TEPD chloride conductance responses in patients with each of the three most common types of nonsense mutations in the CFTR gene. However, the small number of patients included in the interim analysis makes it difficult to draw conclusions based on these observations.

Secondary Endpoint Results. The trials have not been powered to detect statistically significant changes in secondary endpoints. However, in our interim analysis, we observed statistically significant improvements from study entry to the end of the higher-dose treatment cycle in the patients' mean FEV_1, FVC and weight. The following table presents the results of the changes. For the changes in lung function, only 14 of the

15 patients are included because one patient did not have lung function measured at the end of the higher-dose treatment cycle.

Endpoint	Study Entry	End of Higher Dose Treatment	Change	p-Value
Lung function (expressed as a percentage of normal for gender, age and height):				
Mean FEV_1	65.8%	69.1%	3.3%	0.015
Mean FVC	80.2%	85.1%	4.9%	0.037
Weight	58.3 kg	59.0 kg	0.7 kg	0.012

In addition, although we are not formally measuring changes in patient's symptoms through the use of a quality-of-life questionnaire, trial investigators were requested to ask about changes in patients' cystic fibrosis symptoms. In the 15 patients included in the interim analysis, six reported general improvements in well being, six reported decrease in cough and 10 reported decreased mucus thickness and easier clearing of mucus.

Safety and Tolerability Results. PTC124 was generally well tolerated among the 15 patients included in the interim analysis. No serious drug-related adverse events were reported. All adverse events that were potentially drug-related were mild in severity. These adverse events included irritation in the back of the throat in one patient; nausea in two patients; diarrhea in two patients; and dysuria, a burning sensation during urination, in four patients. There were no safety concerns identified in patients' physical examinations, vital sign measurements or electrocardiograms. We did not observe any meaningful elevations in serum liver enzymes or bilirubin. Similarly, we did not observe any clinically relevant changes in kidney function. There were no dosing interruptions or trial discontinuations due to toxicity. Treatment compliance was very good, with patients taking more than 98% of the intended total drug treatment at both the lower and higher dose levels.

Pharmacokinetics. In the patients included in the interim analysis, PTC124 was readily absorbed and desired plasma concentrations were achieved at the first and fourteenth days of both the lower-dose and higher-dose treatment cycles. At both the lower dose level and higher dose level, there was neither evidence of drug accumulation nor evidence of decreased drug levels due to the induction of metabolism during the treatment periods.

Phase 2 Clinical Trial for Duchenne Muscular Dystrophy. In the fourth quarter of 2005, we also commenced an open-label Phase 2 clinical trial of PTC124 for the treatment of Duchenne muscular dystrophy caused by nonsense mutations. The goals of this trial are to obtain indications of pharmacological activity and to assess dose response, safety and pharmacokinetics. We expect to enroll at least 24 evaluable patients age five years or older who have been diagnosed with Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene. We are conducting the trial in the United States at three academic centers that are experienced in the conduct of clinical trials involving subjects with muscular dystrophy.

Participants in the trial are divided into two groups, with all participants in both groups receiving PTC124 treatment for 28 days. The first group comprises the first six participants in the trial. Participants in this group will take PTC124 for 28 days at a dosing regimen consisting of 4 mg/kg with breakfast, 4 mg/kg with lunch and 8 mg/kg with dinner, for a total daily dose of 16 mg/kg. If the six participants in the first group tolerate the study medication, the second group, comprising the remaining participants in the trial, will receive treatment at an escalated dose. For this second group, the dosing regimen will consist of 10 mg/kg with breakfast, 10 mg/kg with lunch and 20 mg/kg with dinner, for a total daily dose of 40 mg/kg. These dosing regimens are the same as for the cystic fibrosis trials, which we based on pharmacokinetic modeling from our Phase 1 clinical trials with the goal of achieving plasma concentrations of PTC124 that, based on our preclinical models, we anticipate may have a therapeutic effect. We will test the effects of PTC124 on trial participants at the end of the 28-day treatment cycle and will conduct a follow-up assessment four weeks after the last dose administration.

The primary endpoint in this trial is the change from baseline measurement of dystrophin levels in a biopsy of a muscle in the foot known as the extensor digitorum brevis, or EDB. An absence of dystrophin at baseline is viewed as confirmation of the diagnosis of Duchenne muscular dystrophy. If PTC124 promotes suppression of the nonsense mutation, we expect to observe increases from baseline in study participants' dystrophin levels in the EDB muscle biopsy. Secondary endpoints of the trial include changes in other proteins in the EDB muscle biopsy, changes in muscle strength, time taken to perform specified functions such as walking and climbing steps and compliance with PTC124 treatment. The trial will also assess the safety and pharmacokinetic profiles of PTC124. We expect to complete this trial in the second half of 2006.

Plans for Future Development

Our goal is to advance the clinical development of PTC124 for both cystic fibrosis and Duchenne muscular dystrophy. Accordingly, we intend to conduct pivotal clinical trials to support the filing of an NDA for a particular indication if our Phase 2 clinical trials for that indication are successful. We anticipate conducting a Phase 2b cystic fibrosis clinical trial in Israel involving the patients participating in our current cystic fibrosis trial in Israel. The purpose of this trial will be to assess the safety and pharmacological activity associated with longer-term dosing of PTC124. Subject to our discussions with regulatory authorities, we anticipate commencing Phase 3 pivotal clinical trials for PTC124 in cystic fibrosis while this Phase 2b trial is ongoing. We expect that primary endpoints for future trials in cystic fibrosis would include clinical measures of lung function and that primary endpoints for future trials in Duchenne muscular dystrophy would include clinical measures of muscle function. We are also assessing additional genetic disorders that are characterized by nonsense mutations to determine whether to initiate clinical trials of PTC124 for the treatment of those indications.

PTC299

PTC299 is a novel, orally administered small-molecule compound designed to inhibit the production of VEGF. We discovered PTC299 using our GEMS technology. We are developing PTC299 for the treatment of cancer because the overexpression of VEGF plays a key role in the growth of many types of cancers. In April 2006, we commenced a Phase 1a clinical trial of PTC299 in healthy volunteers in Belgium. If this Phase 1a trial is successful, we plan to initiate a Phase 1b clinical trial of PTC299 in late 2006 in patients with advanced solid tumors whose disease has progressed during therapy or for whom there is no effective therapy available.

Background on Cancer and the Role of VEGF

According to the American Cancer Society, approximately 1.4 million new cancer cases are reported in the United States annually. Despite significant ongoing drug development aimed at cancer treatment, cancers of all types result in approximately 570,000 deaths in the United States each year, making cancer the second leading cause of death in the United States. VEGF is a protein that stimulates the process of new blood vessel formation, known as angiogenesis. By binding to its receptors on the surface of blood vessel cells, VEGF stimulates blood vessel growth. VEGF overexpression by tumors is critically important in the processes of tumor growth and metastasis for virtually all tumor types. Overexpression of VEGF also plays a role in other diseases, including ophthalmic diseases such as age-related macular degeneration.

Because of the role of VEGF in cancer and other diseases, there has been significant drug discovery activity focused on identifying drugs that target VEGF and its function with the goal of curtailing pathological angiogenesis. Most anti-VEGF compounds that are on the market or under development are designed to prevent VEGF from binding to its receptors, rather than to inhibit the formation of VEGF itself. For example, this is the mechanism of action of Genentech, Inc.'s monoclonal antibody, Avastin. The FDA recently approved Avastin for use in combination with chemotherapy for the treatment of colorectal cancer. Genentech reported that U.S. sales of Avastin were $1.1 billion in 2005. Although Avastin has been successful in slowing the time of tumor progression, the drug does not eradicate cancers. Accordingly, there is an unmet medical need for agents that either eliminate tumors or further reduce the pace of tumor progression. We believe that targeting VEGF by a different mechanism of action may work in a complementary manner with Avastin and other cancer therapies.

PTC299 Scientific Background

Post-transcriptional control processes play a critical role in VEGF production. The initiation of protein translation in most cases depends upon the interaction of ribosomes and associated factors at the end of the mRNA from which translation commences. This mRNA structure is designated as the five prime cap, or 5' cap, and the untranslated region to which the 5' cap is attached is designated as the five prime UTR, or 5' UTR, of the mRNA. Normal translation usually requires the 5' cap. This cap-dependent translation is largely suppressed under conditions of cell stress, such as the occurrence of subnormal concentrations of oxygen, a state known as cell hypoxia. However, the 5' UTR of the mRNA that is used in the formation of VEGF contains a sequence, known as a cellular internal ribosomal entry site, or IRES, that initiates the synthesis of VEGF independently of normal cap-dependent translation. In fact, IRES-dependent VEGF translation increases in the presence of cell hypoxia. As a result, under the hypoxic conditions commonly found in tumors, there is an increase in the amount of VEGF produced. This increased production of VEGF can lead to the subsequent angiogenesis that supports tumor growth.

We have designed PTC299 to inhibit VEGF production in tumors by targeting the post-transcriptional processes that regulate VEGF formation. Based on our preclinical testing, we believe that PTC299 functions through the 5' UTR of the VEGF mRNA. Because PTC299 inhibits VEGF production, its action occurs at a different point in the VEGF pathway than therapies, such as Avastin, that target the binding of VEGF to its receptors on the surface of blood vessel cells. We believe that PTC299 may be active both as a single agent or when used in combination with other anti-angiogenic agents or with chemotherapy agents for the treatment of cancers. PTC299 may also prove clinically useful in other diseases where VEGF levels play a key role, such as in age-related macular degeneration.

Preclinical Development of PTC299

We have conducted multiple *in vitro* and animal preclinical studies of PTC299. Key findings of these studies include the following:

- In *in vitro* studies PTC299 was a potent inhibitor of tumor VEGF production. In these studies, PTC299 demonstrated a broad range of activity in blocking VEGF synthesis in multiple tumor types, including breast, cervical, colorectal, fibrosarcoma, gastric, lung, melanoma, neuroblastoma, ovarian, pancreas, prostate and renal cell cancer lines.
- In multiple animal studies, PTC299 as a monotherapy significantly reduced VEGF concentrations in tumors and plasma, reduced tumor blood vessel density and substantially impeded tumor progression. In addition, in animal studies, PTC299 enhanced the antitumor activity of chemotherapy agents and of Avastin when given as a component of combination therapy.

We believe that safety pharmacology and toxicology studies indicate that PTC299 has an acceptable preclinical safety toxicity profile to proceed to Phase 1a clinical testing in healthy volunteers. *In vitro* and *in vivo* safety pharmacology studies showed no adverse off-target effects and no toxicities in major organ systems. Toxicology studies in rats and dogs through seven days indicated good tolerability at doses and exposures in excess of those required for VEGF inhibition in rats and dogs.

Clinical Development of PTC299

Phase 1a Single-Dose Clinical Trial in Healthy Volunteers. In April 2006, we commenced a Phase 1a clinical trial of PTC299. We have designed this trial as a single-site, randomized, double-blind, placebo-controlled escalating single-dose safety and pharmacokinetic study in healthy volunteers between the ages of 18 and 55. We are conducting this trial in Belgium. We believe that an initial single-dose study of PTC299 in healthy volunteers may allow us to rapidly assess the clinical and pharmacokinetic proprieties of PTC299 in support of a subsequent Phase 1b multiple-dose study in patients with cancer.

We are conducting the Phase 1a trial in two stages. In the first stage, we expect to enroll a total of 40 subjects in five cohorts of eight subjects each. The cohorts will undergo five sequential dose escalations of PTC299. At each treatment administration, six subjects in each cohort will receive a single dose of PTC299

and two subjects will receive a single dose of placebo. We plan to commence the second stage of the trial after we determine the highest safe dose level in the first stage. In the second stage, we expect to enroll 12 new subjects to evaluate the effect of food on the safety and pharmacokinetic profile of PTC299. All participants will take the study medication orally in capsule form. These capsules consist of the active pharmaceutical ingredient of PTC299, in a lipid-soluble form. We are also developing a back-up candidate to PTC299 that may be formulated in a water-soluble form.

The primary objective of this Phase 1a clinical trial is to determine a dose range for PTC299 that is well tolerated, achieves pharmacologically active plasma concentrations and is appropriate for use in a subsequent Phase 1b multiple-dose study. We also expect to assess the side effect profile, drug pharmacokinetics and effects on VEGF concentrations in the blood. We expect to complete this trial in the second quarter of 2006.

Plans for Future Development

If our Phase 1a clinical trial of PTC299 is successful, we plan to initiate a Phase 1b single-arm, open-label, dose-ranging study in late 2006 in patients with advanced solid tumors whose disease has progressed during therapy or for whom there is no therapy available. We expect to conduct this trial in either the United States or Europe.

In this trial, we plan to administer PTC299 to patients in escalating doses in order to determine a maximum tolerated dose. At the maximum tolerated dose, we plan to enroll at least 18 patients to assess the safety of PTC299 and the activity of PTC299 as measured by evaluations of VEGF levels in the blood. We also plan to assess effects on tumor size. The primary objective of this trial will be to establish the maximum tolerated dose and appropriate dose range of PTC299 for application in Phase 2 clinical trials. We expect to complete this Phase 1b trial in late 2007 or early 2008.

If the results of our planned Phase 1a and Phase 1b clinical trials of PTC299 are favorable, we plan to advance PTC299 into additional clinical trials in selected solid tumor indications. We expect to determine those indications based on considerations including scientific rationale, preclinical efficacy, medical need, competitive positioning, patient enrollment potential and the regulatory environment. We anticipate potentially evaluating PTC299 in these clinical trials in combination with chemotherapy, hormonal therapy or anti-angiogenic agents that are typically used to treat the selected indications.

Hepatitis C Program

Using our GEMS technology, we have identified a number of small molecules from our compound library that, in *in vitro* studies, selectively inhibited the translation of the hepatitis C virus protein without inhibiting human host cell translation. In March 2006, we entered into a collaboration with Schering-Plough for the development and commercialization of the compounds in our hepatitis C program. Pursuant to the collaboration, we and Schering-Plough will conduct a joint research program relating to these compounds, and Schering-Plough will be responsible for worldwide development and eventual commercialization efforts for any product candidates that are developed. Schering-Plough has made an upfront payment to us of $12.0 million and has agreed to provide funding for our research activities. In addition, we are eligible to receive more than $200 million in payments if we achieve specified development, regulatory and sales milestones. We are also entitled to royalties on sales of products developed pursuant to the collaboration, with the royalty percentage based on specified thresholds of worldwide net product sales.

Background on Hepatitis C

Hepatitis refers to inflammation of the liver. Hepatitis can result from infection with one of several known viruses, the most common of which are the hepatitis A virus, the hepatitis B virus and the hepatitis C virus. The hepatitis C virus is generally referred to as HCV. Hepatitis A is an acute disease from which individuals typically recover and is rarely fatal. In contrast, hepatitis B and hepatitis C often become chronic, progressive liver disorders, potentially leading to liver scarring, known as cirrhosis, and death from liver failure or liver cancer. Because of the risks associated with hepatitis B and hepatitis C, there is significant drug development effort directed at finding therapeutics for patients with chronic hepatitis B and chronic hepatitis C.

Chronic hepatitis C is the leading cause of liver failure requiring liver transplantation in both the United States and Europe. According to the World Health Organization, approximately 170 million people, or roughly 3% of the world's population, are chronically infected with HCV. The Centers for Disease Control, or CDC, estimate that more than 2.7 million people in the United States have chronic HCV infection. In addition, according to a 1997 National Institutes of Health Consensus Panel Statement, approximately 8,000 to 10,000 patients die annually in the United States from complications resulting from this infection. We expect the prevalence of cirrhosis and the incidence of its complications, including various forms of liver cancer and liver related deaths, to increase dramatically over the next 10 to 20 years. Reports published by Decision Research estimate that the annual worldwide market for hepatitis C therapeutics currently exceeds $3 billion and may exceed $10 billion by 2014.

There are at least six basic genetic variants, or genotypes, of HCV. The different genotypes vary in prevalence in different regions of the world. In the United States, Europe and Japan, the genotype 1 strain of HCV is the most predominant. This genotype is responsible for more than 70% of hepatitis C infections in the United States and Japan and is the predominant HCV genotype in Western Europe. Of the six basic HCV genotypes, the genotype 1 strain is the most difficult to treat with currently available therapies.

There are no available vaccines against HCV. The current standard of care for the treatment of HCV is a combination of two drugs, interferon and ribavirin. More than 50% of patients infected with the genotype 1 strain of HCV generally do not respond to this therapy. In addition, there are significant side effects to this therapy, which often result in dose reductions or premature treatment termination. Product candidates currently in development, such as protease and polymerase inhibitors, have shown rapid development of viral resistance. Thus, there remains a significant unmet medical need for new HCV treatments. We believe that targeting HCV by a different mechanism of action that may work in a complementary manner with other HCV therapies may prove important.

HCV Program Scientific Background

The hepatitis C virus is an RNA virus. The viral genome encodes all of the proteins required for viral reproduction. The HCV RNA does not have a 5' cap structure, but has a large 5' UTR that forms an extensive secondary structure harboring an HCV IRES. The HCV IRES initiates translation using a mechanism that is distinct from the cap-dependent translation involved in normal cellular protein synthesis. The HCV IRES has a critically important function in replication of the HCV virus. As a result, this sequence of RNA is present in all HCV genotypes. This makes the HCV IRES an attractive target for the development of a broad-spectrum anti-HCV agent that is potentially active against all HCV genotypes. Based on our knowledge of the difference between HCV and host cellular protein synthesis, we have designed compounds that have selectively inhibited viral replication in several *in vitro* surrogate cell-based systems. Because the IRES is distinct from viral proteins targeted by existing drugs and other product candidates in development, such as protease or polymerase inhibitors, we believe that our compounds under development may be useful in combination with these other agents. In addition, the essential nature of the IRES may reduce the prospect for resistance to our compounds.

Lead Compound Optimization and Plans for Future Development

We are engaged in late stage chemical optimization of lead compounds in our HCV program. Using our GEMS technology, we have screened our library of compounds to identify a number of potential development candidates that, in *in vitro* testing, specifically inhibited protein synthesis by interacting with the HCV IRES, did not inhibit normal cellular cap-dependent translation and did not display toxicity to cells. Notably, these compounds have displayed equal activity against the IRESs from all common HCV genotypes, including the genotype 1 strain of HCV. Through our collaboration with Schering-Plough, we will continue our research activities with respect to these compounds so that Schering-Plough may select one or more development candidates. Schering-Plough has worldwide clinical development and commercialization rights under the collaboration.

Our Discovery Stage Programs

We believe that targeting post-transcriptional control processes offers opportunities to discover and develop novel therapies for a wide range of diseases. Currently, our most advanced discovery programs are in the areas of antibacterial therapy, anemia and musculoskeletal disorders. In each of these programs we have identified multiple post-transcriptional targets and compounds that have demonstrated *in vitro* and, in many cases, *in vivo* activity. We intend to initiate additional discovery programs in disease areas that we believe to be well suited to our approach and for which we believe there is significant unmet medical need and commercial opportunity.

Our discovery stage programs include the following:

Antibacterial Program

Although currently available antibiotics are effective in treating many bacterial infections, the emergence of resistant strains of bacteria, particularly in the hospital setting, is an increasing worldwide problem. Current therapies do not always address these new resistant strains of bacteria, resulting in a significant unmet medical need for treatments for these new resistant strains of bacteria. We believe that a new broad-spectrum antibiotic directed at a novel target could be an important treatment for bacterial infections.

We have developed a screening technology to identify compounds with the potential to combat infectious bacteria by altering bacterial post-transcriptional control processes. Our most advanced program targets an enzyme known as peptidyl-tRNA hydrolase, or Pth. The Pth enzyme appears to play a key role in a post-transcriptional control process important for all bacteria. We believe that this enzyme is an attractive target because it appears to be essential for bacterial survival. Because the Pth enzyme is present in many types of bacteria, we anticipate that Pth inhibitors could be broad-spectrum antibiotics. Currently there are no drugs that inhibit the Pth enzyme. In *in vitro* tests, the lead compounds in our antibacterial program demonstrated significant activity against several drug-resistant strains of bacteria, including methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* and vancomycin-resistant *Enterococci*. These antibacterial effects have been achieved without toxicity being observed in human cell lines.

Anemia Program

Anemia is a condition that results from a reduced number of red blood cells in circulation, which in turn can lead to insufficient delivery of oxygen to tissues. Common causes of anemia include kidney failure, chronic inflammation, chemotherapy, vitamin deficiency and bleeding. The incidence of anemia has been estimated by DNAPrint Genomics to be as high as 8% in the developed world and higher in the undeveloped world. The hormone erythropoietin, or EPO, is the master regulator of red blood cell production. Increasing the concentration of EPO in the blood is a clinically proven method to alleviate anemia. AS Insights estimates that the worldwide market for recombinant human EPO protein replacement products exceeds $10 billion and is growing at an average annual rate of 21%. All currently approved EPO therapies rely on injection, which is an expensive and inconvenient method of administration. We believe that a small-molecule approach to increasing EPO levels might be able to overcome these disadvantages.

We have applied our GEMS technology to identify small-molecule post-transcriptional activators of EPO gene expression. We have identified several structural classes of small molecules that increase EPO expression in animal models and have favorable pharmaceutical properties.

Musculoskeletal Program

Separate from our development of PTC124 for genetic disorders, we have entered into a collaboration with Parent Project Muscular Dystrophy to identify additional new drugs with the potential to treat Duchenne muscular dystrophy by affecting post-transcriptional control processes. Parent Project Muscular Dystrophy is a patient advocacy organization that supports drug discovery efforts as part of its mission to improve the well being of patients with Duchenne muscular dystrophy. With support from this organization, we have applied our GEMS technology to five different proteins that may be targets for new therapies for patients with

Duchenne muscular dystrophy who would not be candidates for PTC124 treatment because their disease is not caused by a nonsense mutation. In 2004, we performed five high throughput screens against these targets. From these screens, we have identified a number of molecules that demonstrated promising activity in early *in vitro* studies. We are now developing additional data with respect to these targets to begin further characterization of these molecules. This characterization will include preclinical assessment of potency, toxicity and pharmaceutical properties together with chemical optimization. Our goal is to identify appropriate candidates to advance into preclinical and clinical development.

Scientific Background of Post-Transcriptional Control Processes

Proteins are present in all living beings and are essential for the life of each cell as well as the life of the entire organism. To produce proteins, organisms use information encoded in their genes. Genes consist of discrete stretches of DNA molecules located within chromosomes in the nucleus of a cell. Not all of the genes in an organism are used, or expressed, at once. To express a gene and create a protein, the cell follows an ordered, multi-step process.

The first major step in the process of gene expression is called transcription. During transcription, the cell copies the information from a gene to create an RNA molecule that is subsequently processed into a molecule of mRNA. Each mRNA molecule is specific to a particular gene and exists in the cell only for the period it is needed. When present in the cell, the mRNA is used in the next major step of gene expression, called translation. During translation, a specialized cellular apparatus, called the ribosome, decodes the information in each mRNA molecule to produce an individual protein.

Post-transcriptional control processes are the events that occur in cells following the transcription of DNA to make mRNA. These processes include mRNA processing, transport and eventual degradation, as well as translation of mRNA into protein. These processes also modulate how long an mRNA molecule lasts in the cell and how efficiently the mRNA is used to make its protein. The quantity of a particular protein produced in a given time period depends both on how much of the mRNA that codes for that protein is in the cell and on how efficiently the cellular translation apparatus uses that mRNA. Precise control of mRNA utilization is critical for many important functions, including the cell division cycle, the immune response and the growth and repair of tissues.

Portions of mRNA molecules that do not directly code for proteins, known as untranslated regions, or UTRs, are unique to specific mRNAs and are directly involved in the post-transcriptional control of protein production. Interactions of other molecules in the cell with the UTRs and other control structures on the mRNA can modulate the rate at which mRNA is degraded and eliminated from the cell as well as the mRNA's translational efficiency. These regulatory molecules in the cell also often interact with each other. The various post-transcriptional control processes are critical to proper cellular function and provide the organism with a diverse array of approaches to modulate protein levels in response to specific biological needs.

Our Post-Transcriptional Control Drug Discovery Technologies

We have assembled an integrated set of proprietary technologies for the discovery of small molecules that target post-transcriptional control processes. Our technologies allow us to perform multiple screens of our compound library in different therapeutic areas in an expeditious and cost-effective manner. Our scientists are able to conduct a drug discovery program from target identification and characterization to the identification of selective lead molecules with defined pharmaceutical properties within months.

GEMS is the principal technology that we use to identify small-molecule drug candidates that have the potential to up-regulate or down-regulate protein levels. The compounds that we identify using GEMS modulate gene expression by targeting the post-transcriptional control processes that act through the UTRs of mRNA molecules. We have used our GEMS technology in the discovery and development of PTC299 and to identify the lead compounds in our HCV program. Furthermore, we are conducting preclinical testing of a number of compounds in other programs that we have identified through GEMS.

The Importance of UTRs in Post-Transcriptional Control Processes

The mRNA of humans consists of several specific regions. At the beginning of an mRNA molecule is the 5' cap, which is a structure attached to the mRNA through a post-transcriptional process. Adjacent to the 5' cap is the 5' UTR. Located next to the 5' UTR is the open reading frame, which contains the information that the ribosomes decode to produce proteins. The 3' UTR follows the open reading frame. The terminal element of the 3' UTR is a structure known as the poly(A) tail. The following diagram illustrates the mRNA structure.

The UTRs of mRNA have important roles in the regulation of protein production by the cell because they contain the instructions for how much protein should be made from a given mRNA molecule. The information in the UTRs can determine whether one protein molecule is synthesized per mRNA or thousands of copies of a protein are synthesized. The UTRs usually function independently from other elements of mRNA, such as the open reading frame. Our GEMS technology takes advantage of this property of UTRs to identify small molecules that modulate post-transcriptional control.

Our GEMS and Other Discovery Technologies

Before applying our GEMS technology, we seek to identify target proteins of potential biological and medical relevance to human disease. We select targets based on our reviews of the biomedical literature and discussions with our scientific advisors. We analyze each potential target to determine whether its cellular production is likely to be affected by post-transcriptional control processes and to assess the clinical feasibility of developing a therapeutic that acts on the target.

After identifying a target, we precisely identify the UTRs of the gene for that target. We then link the sequences of the UTRs with a reporter gene so that the target gene's UTRs flank the open reading frame of the reporter gene. The following diagram illustrates this process.

In most cases, we derive the reporter from the firefly luciferase gene. Luciferase is a protein that performs a chemical reaction that produces light. Compounds that act at the UTRs to modulate luciferase protein levels increase or decrease the amount of light produced. By measuring changes in the amount of light, we can rapidly assess the effect of a test compound on post-transcriptional processes.

The next step of our GEMS technology is to develop stable cell lines that express the UTR-reporter gene constructs. We test these cell lines against our compound library using high-throughput screening technology. In a typical screen, we assay the effect of the compounds in our library to identify those that are likely to enhance or inhibit expression of the target gene by modulating the post-transcriptional control processes that act through that target's UTRs. We can screen our entire library of approximately 200,000 compounds in one week.

We then select compounds that demonstrate statistically significant alterations in reporter expression for further characterization in secondary assays. These assays monitor the dose-response profile of the compounds, their cell-based activity against the target and their specificity and selectivity against other protein targets. Based on the results of these analyses, and on the compounds' pharmacological activity and toxicity in animal models, we identify lead compounds and initiate chemical lead optimization. The goal of lead optimization is to improve compound efficacy, potency and pharmaceutical properties, so that we can select a development candidate to evaluate in preclinical studies and clinical trials.

We have developed considerable knowledge in the area of post-transcriptional regulation of gene expression. Using this knowledge, we have discovered new elements in UTRs that regulate gene expression and have built databases that allow us to identify targets that are suitable for our technology. We have also

discovered new regulatory mechanisms that require cooperative interaction between sequences situated in both the 5' and 3' UTRs of the mRNA and the proteins that interact with these elements. These cooperative interactions play an essential role in regulating the protein levels of important genes and, we believe, represent new and promising targets for the selective modulation of gene expression in a number of therapeutic areas, including genetic disorders, oncology, infectious diseases, anemia and musculoskeletal disorders, as well as inflammation, metabolic disorders, cardiovascular conditions and neurological disorders.

We believe that our GEMS technology enables us to identify small-molecule compounds that alter protein production for previously intractable target proteins and target proteins that have not yet been isolated or structurally characterized. In addition, we believe that a key advantage of our GEMS technology is that it is commercially scalable. In particular, we can screen a large number of medically relevant targets in a short period of time and continually add targets to the screening tier.

In addition to GEMS, we have developed several other proprietary approaches to identify compounds with the potential to treat disease by interacting with post-transcriptional control processes. For example, we discovered PTC124 using an approach that identifies compounds that can overcome a nonsense mutation in the open reading frame of a reporter gene. In addition, our antibacterial program stems from a drug discovery platform we developed that identifies compounds directed against the synthesis or metabolism of a type of RNA, called transfer RNA, that is required for protein synthesis.

Our Compound Library

We believe that our compound library of approximately 200,000 diverse compounds is another important asset of our drug discovery and development efforts. We designed this library to maximize diversity and drug-like characteristics relevant to the targeting of post-transcriptional control processes. We support the library with an automated infrastructure for compound handling and housing, thereby allowing rapid and accurate robotic integration of this chemistry resource with our drug discovery technologies.

Integrated Research and Development Infrastructure

We have integrated the biology, chemistry, pharmacology and clinical aspects of our drug discovery and development activities. To do so, we employ extensive and sophisticated informatics across biology and chemistry and multiple predictive approaches to target identification, compound analoging and lead optimization. We believe that the integration of these disciplines enhances the speed, efficiency and yield of our drug discovery processes. Using this infrastructure, we have established a large, proprietary dataset pertaining to the activity of our compound library. We routinely perform computational analysis of this dataset, which allows us to rapidly identify compounds that demonstrate specificity against a desired target. This capability enables us to quickly progress from the initial stage of screening compounds to the identification and optimization of chemical hits from those screens. As we assess pharmacological properties, such as bioavailability, metabolism and pharmacokinetics, we integrate this information into a database so that we can subsequently compare large numbers of compounds and select those with the most desirable properties. During this process, there is frequent consultation among our biology, chemistry, pharmacology and clinical disciplines so that we select final development candidates we believe will demonstrate the desired characteristics when advanced into preclinical and clinical development.

Use of Pharmacodynamic Markers in Clinical Trials

In our development activities, we generally focus on indications for which there are well-defined pharmacodynamic markers that can serve as measurements of efficacy, or endpoints, in human clinical trials. Pharmacodynamic markers generally are cellular or tissue functions, enzyme activities or protein levels that are indicative of clinical improvement of the underlying disease. Although the FDA typically requires more direct measures of clinical improvement in later stage clinical trials, the benefit of pharmacodynamic markers is that they can allow for a rapid determination of signals of potential drug function in early-stage clinical trials. One of the reasons that we chose cystic fibrosis and Duchenne muscular dystrophy as our initial target indications for PTC124 is that there are well-established pharmacodynamic markers for both of these

disorders. There are also pharmacodynamic markers for the anti-VEGF mechanism of action of PTC299, and viral load may be a pharmacodynamic marker in clinical trials for any HCV product candidates that result from our collaboration with Schering-Plough.

Our Strategy

Our goal is to become a leading pharmaceutical company focused on developing and commercializing small-molecule therapeutics that target post-transcriptional control processes and address unmet medical needs. To achieve our goal, we are pursuing the following strategies:

- ***Rapidly advance our lead programs.*** We are devoting a significant portion of our resources and business efforts to completing the development of our most advanced product candidates. We plan to complete our Phase 2 clinical trials of PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy and advance this product candidate into pivotal clinical trials as rapidly as possible. In addition, we believe that PTC124 may have applicability to a significant number of other genetic disorders for which a nonsense mutation is the cause of the disease. Similarly, we believe that PTC299, our anti-angiogenesis product candidate, may have potential to treat a range of solid tumor cancers as well as other diseases in which angiogenesis and VEGF overexpression play a role, such as age-related macular degeneration. We plan to pursue these additional potential commercial opportunities for PTC124 and PTC299 aggressively. For our genetic disorder program with PTC124, we are collaborating with patient advocacy groups, foundations and government agencies in order to obtain financial support, access to thought leaders and assistance in obtaining market acceptance of products that we successfully develop. We plan to pursue similar activities in other programs.
- ***Apply our integrated approach to continue to discover and develop small molecules that alter post-transcriptional control processes.*** We are applying several proprietary technologies, including GEMS, to the discovery and development of small molecules designed to exert therapeutic effects by altering post-transcriptional control processes. We have steadily enhanced these technologies, which span the key disciplines of biology, chemistry and pharmacology, over a number of years. Because post-transcriptional control processes offer many targets for therapeutic intervention and because drugs that alter these processes have the potential to both up-regulate and down-regulate protein production, we believe that our approach may be applicable to a broad range of diseases. We plan to continue to build our technologies for application in the field of post-transcriptional control processes and to apply these technologies in discovering and developing treatments in new therapeutic areas.
- ***Build a specialized sales and marketing infrastructure.*** We plan to establish our own sales and marketing capabilities. We expect to accomplish this initially by retaining commercial rights for our product candidates for which we receive marketing approvals in situations in which we believe it is possible to access the market through a focused, specialized sales force. For example, for PTC124, we believe that the pulmonologists and neurologists who are the key specialists in treating cystic fibrosis and Duchenne muscular dystrophy are sufficiently concentrated that we will be able to effectively promote the product with our own targeted sales force. For some situations in which we enter into commercial collaborations with third-party pharmaceutical and biotechnology companies, our goal will be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets, in order to further develop our internal sales and marketing capabilities.
- ***Selectively establish strategic alliances with leading pharmaceutical and biotechnology companies.*** For each of our product candidates, we plan to evaluate the merits of retaining commercialization rights for ourselves or entering into collaboration arrangements with leading pharmaceutical or biotechnology companies, such as our collaborations with Schering-Plough and Bausch & Lomb. Our decision to enter into additional collaboration arrangements will be based on such factors as anticipated development costs, therapeutic expertise and the commercial infrastructure required to access a particular market. We generally plan to seek collaborators for the development and commercialization of product candidates that have high anticipated development costs or that are

directed at indications for which a potential collaborator has a particular expertise or that involve markets that can be served more effectively by a large sales and marketing organization.

Our Collaborations

A key element of our strategy is to establish strategic collaborations with leading pharmaceutical and biotechnology companies. To date, we have entered into collaborations with Schering-Plough Corporation and Bausch & Lomb. These collaborations provide us with an opportunity to extend our post-transcriptional drug discovery technology into additional therapeutic areas and to benefit from the research, development and commercialization capabilities of our collaborators as well as to augment our financial resources.

Schering-Plough

In March 2006, we entered into a collaboration and license agreement with a subsidiary of Schering-Plough Corporation under which we and Schering-Plough are collaborating in the discovery, development and commercialization of compounds for the treatment of HCV and other viral diseases. Pursuant to the collaboration agreement, Schering-Plough paid us an upfront non-refundable payment of $12.0 million. Schering-Plough has additional financial obligations described below.

Research Collaboration. The agreement provides for a research collaboration under which we and Schering-Plough will conduct a research program designed to discover, identify, synthesize and evaluate our compounds for use in the prevention, treatment or diagnosis of HCV. During the research term, Schering-Plough has agreed to provide us with funding, based on a full-time equivalent rate, for an agreed upon number of full-time equivalent scientific or research and development personnel that we dedicate to the research program. The initial research term is three years. Schering-Plough has two options to extend the research term for an additional term of one year per option. Schering-Plough can terminate the research term in the circumstances described below.

Development and Commercialization. Schering-Plough is responsible for worldwide clinical development and commercialization of any compounds that it elects to advance from our research collaboration. We have granted Schering-Plough worldwide exclusive licenses, with the right to grant sublicenses, to our patent rights and know-how with respect to compounds arising from the collaboration that exhibit high anti-HCV activity. We are eligible to receive more than $200 million in payments if specified development, regulatory and sales milestones are achieved. Some of these milestones relate to second products or indications. We are also entitled to royalties on sales of products developed pursuant to the collaboration, with the royalty percentage based on specified thresholds of worldwide net product sales. Schering-Plough's obligation to pay us royalties at full rates will expire generally on a country-by-country basis on the expiration of the last-to-expire patent covering a product in the given country. In some circumstances following the expiration of all applicable patents in a particular country, Schering-Plough may be obligated to pay us royalties at lower rates for a specified period following the launch of the product in the country.

Exclusivity. Schering-Plough has the exclusive right to develop and commercialize compounds arising from the collaboration that exhibit high anti-HCV activity. Furthermore, for a period ending on the one-year anniversary of the expiration or termination of the research term, except in the case of certain terminations of the collaboration agreement or in the event that Schering-Plough in-licenses or acquires certain compounds or products, neither we nor Schering-Plough is permitted, outside the collaboration, to conduct any research or development on compounds that have as their primary mechanism of action the inhibition, either directly or indirectly, of viral replication by virtue of decreasing IRES-dependent translation of viral proteins.

Termination. Unless terminated earlier, the collaboration agreement will continue on a country-by-country and a product-by-product basis until there are no remaining royalty payment obligations in the given country with respect to the particular product.

Schering-Plough's termination rights under the collaboration agreement include the following:

- the right to terminate the collaboration agreement upon prior written notice at any time after the third anniversary of the effective date of the agreement;

- the right to terminate the collaboration agreement if, during the research term, a third-party patent or patent application that could substantially interfere with compounds that we are pursuing under the research collaboration is granted or published in a major market and we are not able to mutually agree on an applicable course of action or obtain a non-infringement opinion with respect to such patent or patent application; and
- the right to terminate the research program or the collaboration agreement upon prior written notice if Schering-Plough has not accepted a development candidate within two years of the effective date of the agreement.

Either party may terminate the collaboration agreement in the event of an uncured material breach by the other party or in the event of the other party's bankruptcy or insolvency. In addition, Schering-Plough has the right to terminate the research program upon specified changes of control of us involving competitors of Schering-Plough.

Upon termination of the collaboration agreement in specified circumstances, including termination by Schering-Plough for convenience or termination by us as a result of Schering-Plough's breach or bankruptcy, we have the right to assume the development and commercialization of product candidates arising from the collaboration agreement. In that event, we may become obligated to pay royalties to Schering-Plough on net sales of any products for which we receive regulatory approvals.

Joint Steering Committee. The collaboration is governed by a joint steering committee, consisting of an equal number of representatives of us and Schering-Plough. The parties have agreed to use reasonable good faith efforts to reach consensus on all decisions within the responsibility of the joint steering committee. If the parties cannot reach agreement, including, in the case of decisions relating to the research collaboration, after following a specified decision resolution procedure, Schering-Plough's decision will control. However, Schering-Plough may not make decisions relating to the research collaboration that are inconsistent with Schering-Plough's funding obligations, that would require us to undertake specified research activities unrelated to the optimization or characterization of the compounds being pursued under the collaboration, or that would prevent us from presenting for designation a development candidate or a back-up development candidate.

Bausch & Lomb

In December 2005, we entered into a research collaboration and exclusive option agreement with Bausch & Lomb under which Bausch & Lomb is evaluating compounds from our anti-angiogenesis program for the purpose of identifying potential candidates for development by Bausch & Lomb for the treatment of ophthalmic diseases associated with angiogenesis, including macular degeneration. Under the terms of the agreement, we granted Bausch & Lomb the exclusive option to license specified compounds, which we refer to as the program compounds, for the treatment, diagnosis or prevention of diseases of the eye. If Bausch & Lomb exercises its option for any of the program compounds, Bausch & Lomb would be obligated to pay us an option exercise fee and we and Bausch & Lomb would enter into a license agreement in a pre-negotiated form. Under any such license, we would be eligible to receive up to $17.5 million in payments based on the achievement of specified development, regulatory and sales milestones with respect to the first compound developed under the applicable license. We would also be entitled to receive royalties on sales of products developed pursuant to any such license, with the royalty percentage based on specified thresholds of worldwide net product sales. In addition, we granted Bausch & Lomb the exclusive option to license specified alternative compounds, which we refer to as the development compounds, for the treatment, diagnosis or prevention of diseases of the eye through local delivery to the eye. If Bausch & Lomb exercises its option for any of the development compounds, we and Bausch & Lomb would enter into a license agreement on terms, including financial terms, to be negotiated. If we and Bausch & Lomb are not able to reach agreement on license terms for the development compounds within a specified period, Bausch & Lomb's option to license the development compounds will expire. Bausch & Lomb has one year from the date of the agreement to exercise any of its license options.

In exchange for the one-year options, Bausch & Lomb paid us an upfront non-refundable option grant fee of $300,000 and agreed to provide us with research funding during the option term to compensate us for completing agreed research. Bausch & Lomb has the right to extend the option term with respect to the program compounds for an additional six months in exchange for an extension fee. Either we or Bausch & Lomb may terminate the agreement in the event of the other party's uncured material breach of the agreement. Bausch & Lomb may terminate the agreement without cause upon 90 days' written notice to us. Upon expiration of Bausch & Lomb's license options, the rights to compounds that Bausch & Lomb has not elected to license revert to us.

Intellectual Property

Patents and Trade Secrets

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of December 31, 2005, we owned or exclusively licensed a total of 15 U.S. patents and 38 U.S. patent applications as well as numerous foreign counterparts to many of these patents and patent applications. Our patent portfolio includes patents and patent applications with claims directed to the composition of matter, pharmaceutical formulation and methods of use of many of our compounds, including PTC124 and PTC299.

The patent rights relating to PTC124 owned or licensed by us consist of one issued U.S. composition of matter patent and multiple patent applications relating to composition of matter, methods of use, formulation and dosing. The issued patent is currently set to expire in 2024 and all U.S. patents that issue from the pending U.S. patent applications would currently expire in 2024, except for one, which would expire in 2026. All of these patent rights are also the subject of counterpart patent applications in a number of other jurisdictions, including Europe and Japan. The patent rights relating to PTC299 owned by us consist of two U.S. patent applications and one counterpart PCT patent application which designates other jurisdictions, including Europe and Japan. These patent applications relate to the composition of matter, methods of use and formulation of PTC299. Any U.S. patents that issue from the pending U.S. patent applications relating to PTC299 would currently expire in 2025. U.S. patents generally have a term of 20 years from the filing date of the earliest non-provisional application.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, narrowed, circumvented or found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. Neither we nor our licensors can be certain that we were the first to invent the inventions claimed in our owned or licensed patents or patent applications. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us, and the rights granted under any issued patents may not provide us with any meaningful competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by

confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures 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 consultants, contractors or collaborators 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.

License Agreements

We are a party to a number of license agreements under which we license patents, patent applications and other intellectual property. We enter into these agreements to augment the significant intellectual property created by our scientists. The licensed intellectual property covers some of the compounds that we are researching and developing, some post-transcriptional control targets and some of the scientific processes that we use. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of PTC124 or PTC299 or for the compounds that we are testing in our preclinical programs. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any products that we may develop, other than small amounts of compounds that we synthesize ourselves for preclinical testing. To date, we have obtained our supply of the bulk drug substance for both PTC124 and PTC299 from one third-party manufacturer. We engaged a second manufacturer to provide the fill and finish services for the finished product that we are using in our ongoing Phase 2 clinical trials of PTC124 and our Phase 1a clinical trial of PTC299. We are in the process of negotiating an agreement with a new manufacturer for the supply of bulk drug substance for our future clinical trials of PTC124 and PTC299. We obtain our supplies of the product candidates from these manufacturers pursuant to agreements that include specific supply timelines and volume expectations. If any of these manufacturers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might incur some delay in identifying and qualifying such replacements.

All of our drug candidates are organic compounds of low molecular weight, generally called small molecules. We have selected these compounds not only on the basis of their potential efficacy and safety, but also for their ease of synthesis and reasonable cost of their starting materials. In particular, PTC124 and PTC299 are each manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining

qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

If PTC124, PTC299 or an HCV product candidate are approved, they will compete with currently marketed drugs and potentially with other product candidates that are currently in development for the same indications. The competition for our product candidates includes the following:

- ***PTC124 for cystic fibrosis.*** There are currently no approved therapeutics to treat the root causes of cystic fibrosis. Current treatments are designed to alleviate the symptoms of the disease and depend upon the stage of the disease and the organs involved. Clearing mucus from the lungs is an important part of the daily cystic fibrosis treatment regimen. Chest physical therapy is a form of airway clearance that involves vigorous clapping on the back and chest to dislodge the thick mucus from the lungs. Other treatments for cystic fibrosis include TOBI, an aerosolized antibiotic used to treat lung infections that is marketed by Chiron Corporation, Pulmozyme, a mucus-thinning drug shown to reduce the number of lung infections and improve lung function, that is marketed by Genentech, Inc., and azithromycin, an antibiotic recently proven to be effective in people with cystic fibrosis whose lungs are chronically infected with the common bacteria known as *Pseudomonas aeruginosa*. We believe that PTC124 is the only orally administered product candidate in clinical trials that is designed to treat the root cause of cystic fibrosis by restoring CFTR activity through the read through of a nonsense mutation. However, we are aware of other preclinical and clinical programs of third parties aimed at modulating CFTR function, including programs of Alnylam Pharmaceuticals, Inc. and Vertex Pharmaceuticals Incorporated. In addition, various other anti-inflammatory, anti-infective and mucus regulating product candidates are in clinical development.
- ***PTC124 for Duchenne muscular dystrophy.*** There are currently no approved therapeutics to treat the root causes of Duchenne muscular dystrophy. Current treatments seek to address symptoms through supportive care measures, such as bracing, joint stretching exercises, tendon release surgery, wheelchair use and assisted ventilation. Corticosteroids, such as prednisone and deflazacort are often prescribed to treat some of the symptoms of the disease. We believe that PTC124 is the only product candidate in clinical trials that is designed to treat the root cause of Duchenne muscular dystrophy by restoring dystrophin activity through the read through of a nonsense mutation. We are aware of early stage gene therapy programs of third parties targeting Duchenne muscular dystrophy. Various growth factors in development for other indications, including other forms of muscular dystrophy and amyotrophic lateral sclerosis, may, if approved, be used for the treatment of Duchenne muscular dystrophy. In addition, Wyeth has a potentially muscle-enhancing product candidate in Phase 2 clinical trials for muscular dystrophy.
- ***PTC299.*** If approved for the treatment of cancer, PTC299 would compete with numerous cancer therapies. Most notably, we expect that PTC299 would compete with other anti-angiogenesis therapies. These include Genentech's Avastin and Bayer's and Onyx's Nexavar, which act by preventing VEGF from binding to its receptor, and Pfizer Inc.'s Sutent, a tyrosine kinase inhibitor. We are also aware of numerous other anti-angiogenesis cancer therapies in development by third parties, including the VEGF Trap, which is in development by Sanofi-Aventis and Regeneron. However, we are not aware of any other product candidates that, like PTC299, are designed to prevent VEGF formation by targeting post-transcriptional control processes.
- ***HCV.*** The current standard of care for the treatment of HCV is the combination of interferon and ribavirin. In addition, there are numerous product candidates for the treatment of HCV in clinical

development. These include product candidates of Idenix Pharmaceuticals, Inc. and Vertex Pharmaceuticals.

The key competitive factors affecting the success of all of our product candidates are likely to be their efficacy, safety, convenience and price.

Sales and Marketing

If we receive regulatory approval for our product candidates, we plan to commence commercialization activities by building a focused sales and marketing organization complemented by selective co-promotion and other arrangements with leading pharmaceutical or biotechnology collaborators.

We generally expect to retain commercial rights for our product candidates for which we receive marketing approvals in situations in which we believe it is possible to access the market through a focused, specialized sales force. In particular, we believe that such a sales force could address the community of pulmonologists and neurologists who are the key specialists in treating cystic fibrosis and Duchenne muscular dystrophy, for which we are developing PTC124. Accordingly, if PTC124 is approved, we plan to initially build our own internal sales force to target these specialists.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with thought leaders in relevant fields of medicine.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, approval, manufacturing, labeling, post-approval monitoring and reporting, packaging, promotion, storage, advertising, distribution, marketing and export and import of pharmaceutical products such as those we are developing. The process of obtaining regulatory approvals and the subsequent substantial compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the information that must be submitted to the FDA in order to obtain approval to market a new drug varies depending upon whether the drug is a new product whose safety and efficacy have not previously been demonstrated in humans or a drug whose active ingredients and certain other properties are the same as those of a previously approved drug. A product whose safety and efficacy have not previously been demonstrated in humans will follow the New Drug Application, or NDA, route.

The NDA Approval Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act and implementing regulations. Failures to comply with the applicable FDA requirements at any time during the product development process, approval process or after approval may result in administrative or judicial sanctions. These sanctions could include the FDA's imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

The steps required before a drug may be marketed in the United States include:

- completion of preclinical laboratory tests, animal studies and formulation studies under the FDA's good laboratory practices regulations;

- submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin and which must include independent Institutional Review Board, or IRB, approval at each clinical site before the trials may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with Good Clinical Practices to establish the safety and efficacy of the product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical testing may continue after the IND is submitted. The IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. In other words, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each site at which the study is conducted must approve the protocol and any amendments. All research subjects must provide their informed consent in writing.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Phase 1 trials usually involve the initial introduction of the investigational drug into healthy volunteers to evaluate the product's safety, dosage tolerance and pharmacokinetics and, if possible, to gain an early indication of its effectiveness.

Phase 2 trials usually involve controlled trials in a limited patient population to:

- evaluate dosage tolerance and appropriate dosage;
- identify possible adverse effects and safety risks; and
- provide a preliminary evaluation of the efficacy of the drug for specific indications.

Phase 2 trials are sometimes denoted by companies as Phase 2a or Phase 2b trials. Phase 2a trials typically represent the first human clinical trial of a drug candidate in a smaller patient population and are designed to provide earlier information on drug safety and efficacy. Phase 2b trials typically involve larger numbers of patients or longer durations of therapy and may involve comparison with placebo, standard treatments or other active comparators.

Phase 3 trials usually further evaluate clinical efficacy and test further for safety in an expanded patient population. Phase 3 trials usually involve comparison with placebo, standard treatments or other active comparators. These trials are intended to establish the overall risk-benefit profile of the product and provide an adequate basis for physician labeling. Phase 3 trials are usually larger, more time consuming, more complex and more costly than Phase 1 and Phase 2 trials.

Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. Furthermore, the FDA or we may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of research if the research is not being conducted in accordance with the IRB's requirements or if the research has been associated with unexpected serious harm to patients.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical trials, together with other detailed information, including information on the chemistry, manufacture and composition of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. In most cases, the NDA must be accompanied by a substantial user fee. The FDA will initially review the NDA for completeness before it accepts the NDA for filing. After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether a product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity.

Under the Pediatric Research Equity Act of 2003, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Before approving an NDA, the FDA will inspect the facility or the facilities at which the product is manufactured. The FDA will not approve the product unless cGMP compliance is satisfactory. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our products. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the products. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

After regulatory approval of a product is obtained, we are required to comply with a number of post-approval requirements. For example, as a condition of approval of an NDA, the FDA may require post marketing testing and surveillance to monitor the product's safety or efficacy. In addition, holders of an approved NDA are required to report certain adverse reactions and production problems to the FDA, to provide updated safety and efficacy information and to comply with requirements concerning advertising and promotional labeling for their products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes certain procedural, substantive and recordkeeping requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future FDA inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require

substantial resources to correct. In addition, discovery of problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications. Also, new government requirements, including those resulting from new legislation, may be established that could delay or prevent regulatory approval of our products under development.

Orphan Drug Designation

We have received an orphan drug designation from the FDA for our product candidate PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy resulting from a nonsense mutation. The FDA may grant orphan drug designation to drugs intended to treat a "rare disease or condition" that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Orphan drug designation can provide opportunities for grant funding towards clinical trial costs, tax advantages and FDA user-fee benefits. In addition, if a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors may receive approval of different drugs or biologics for the indications for which the orphan product has exclusivity.

Fast Track Designation

We have obtained fast track designation from the FDA for our product candidate PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy caused by nonsense mutations. The FDA's fast track programs, one of which is fast track designation, are designed to facilitate the development and review of new drugs that are intended to treat serious or life threatening conditions and that demonstrate the potential to address unmet medical needs for the conditions. Fast track designation applies to a combination of the product and the specific indication for which it is being studied. Thus, it is the development program for a specific drug for a specific indication that receives fast track designation. The sponsor of a product designated as being in a fast track drug development program may engage in close early communication with the FDA including through timely meetings and feedback on clinical trials. Products in fast track drug development programs also may receive priority review or accelerated approval and sponsors may be able to submit portions of an application before the complete application is submitted. The FDA may notify a sponsor that its program is no longer classified as a fast track development program if the fast track designation is no longer supported by emerging data or the designated drug development program is no longer being pursued.

Regulation Outside the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the United States before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

We have obtained an orphan medicinal product designation from the Committee for Orphan Medicinal Products of the EMEA for our product candidate PTC124 for the treatment of cystic fibrosis and Duchenne muscular dystrophy. The EMEA grants orphan drug designation to promote the development of products that

may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free protocol assistance, fee reductions for access to the centralized regulatory procedures before and during the first year after marketing authorization and 10 years of market exclusivity following drug approval. Fee reductions are not limited to the first year after authorization for small and medium enterprises. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

To obtain regulatory approval of a drug under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes and optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. All marketing authorizations for products designated as orphan drugs must be granted in accordance with the centralized procedure. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state’s assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

Pharmaceutical Pricing and Reimbursement

In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare product candidates. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. Our product candidates may not be considered cost-effective. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In 2003, the United States government enacted legislation providing a partial prescription drug benefit for Medicare recipients, beginning in 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through drug procurement organizations operating pursuant to this legislation. These organizations would negotiate prices for our products, which are likely to be lower than we might otherwise obtain. Federal, state and local governments in the United States continue to consider legislation to limit the growth of healthcare costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as the drug candidates that we are developing.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In

addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on pharmaceutical pricing.

Scientific Advisory Board

Our scientific advisory board consists of scientific and clinical advisors who are leading experts in the fields of post-transcriptional regulation and chemistry, preclinical studies, drug manufacturing or clinical trials. Our scientific advisory board consults with us regularly on matters relating to:

- our research and development programs;
- the design and implementation of our clinical trials;
- market opportunities from a clinical perspective;
- new technologies relevant to our research and development programs; and
- scientific and technical issues relevant to our business.

Our current scientific advisory board members are:

Name	Professional Affiliation
Allan Jacobson, Ph.D.	Chairman of the Department of Molecular Genetics and Microbiology, University of Massachusetts Medical School
Eric N. Jacobsen, Ph.D.	Professor, Department of Chemistry and Chemical Biology, Harvard University
Paul A. Marks, M.D.	President Emeritus and Head, Developmental Cell Biology Laboratory, Memorial Sloan-Kettering Cancer Center
Joseph Puglisi, Ph.D.	Professor and Chair, Department of Structural Biology and Director of the Stanford Magnetic Resonance Laboratory, Stanford University School of Medicine
Robert Schneider, Ph.D.	Professor, Department of Microbiology, Program in Microbiology, Cellular and Molecular Biology, Molecular Oncology and Immunology, and co-director of translational cancer research and breast cancer research programs, New York University School of Medicine
H. Lee Sweeney, Ph.D.	Professor and Chairman of Physiology, University of Pennsylvania School of Medicine
Marvin Wickens, Ph.D.	Professor of Biochemistry, University of Wisconsin-Madison; former President of the RNA Society

Employees

As of March 15, 2006, we had 91 full-time employees, including a total of 42 employees with M.D. or Ph.D. degrees. Of our workforce, 62 employees are engaged in research and development. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Properties

Our principal facilities consist of approximately 42,000 square feet of research and office space located at 100 and 200 Corporate Court, Middlesex Business Center, South Plainfield, New Jersey that we occupy under a lease that expires in 2009. We have an option to renew this lease for an additional five years.

Legal Proceedings

We are not currently a party to any material legal proceedings.

MANAGEMENT

Our executive officers and directors and their respective ages and positions as of March 15, 2006 are as follows:

Name	Age	Position
Stuart W. Peltz, Ph.D.	46	President and Chief Executive Officer and Director
William D. Ju, M.D.	49	Chief Operating Officer
Langdon Miller, M.D.	52	Chief Medical Officer
William Baird, III	34	Chief Financial Officer
John Babiak, Ph.D.	49	Senior Vice President, Drug Discovery Technologies
Mark E. Boulding	45	Senior Vice President and General Counsel
Michael Schmertzler(2)(3)	54	Chairman of the Board of Directors
Harvey Berger, M.D.(2)	55	Director
Axel Bolte(2)	34	Director
Søren Carlsen, Ph.D.	53	Director
Carl Goldfischer, M.D.(1)(3)	47	Director
Allan Jacobson, Ph.D.	60	Director
Michael Kranda(1)	52	Director
David P. Southwell(1)(3)	45	Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Corporate Governance Committee.

Stuart W. Peltz, Ph.D. is a co-founder of our company and has been our President and Chief Executive Officer and a member of our board of directors since our inception in 1998. Prior to founding PTC, Dr. Peltz was a Professor in the Department of Molecular Genetics & Microbiology at the University of Medicine and Dentistry of New Jersey. Dr. Peltz has published over 80 publications in the area of post-transcriptional control processes. Dr. Peltz received his Ph.D. from the McArdle Laboratory for Cancer Research at the University of Wisconsin.

William D. Ju, M.D. has been our Chief Operating Officer since October 2003. From July 2001 to September 2003, Dr. Ju was the Vice President, Research and Development and Project Leadership Oncology of Pharmacia Corporation, a pharmaceutical company. From May 1994 to June 2001, Dr. Ju held executive positions at Merck Research Laboratories in clinical pharmacology, clinical research, regulatory affairs and project planning in numerous therapeutic areas. From May 1992 to April 1994, Dr. Ju was a clinical leader developing new chemical entities and supporting marketed compounds at Hoffmann-La Roche. From July 1988 to April 1992, Dr. Ju was a senior staff fellow in basic oncology research at the National Cancer Institute. Dr. Ju received his M.D. degree from the University of Pennsylvania School of Medicine, where he completed his residency and chief residency training.

Langdon Miller, M.D. has been our Chief Medical Officer since July 2003. From 1995 until July 2003, Dr. Miller served in various positions in oncology clinical development, including as Vice President of Global Clinical Research, Oncology, at Pharmacia Corporation. From 1989 to 1995, Dr. Miller served as a Senior Investigator at the National Cancer Institute. Dr. Miller received his M.D. degree from Northwestern University Medical School. He completed an internal medicine residency at the University of Minnesota and a medical oncology fellowship at Stanford University.

William Baird, III has been our Chief Financial Officer since April 2005. From February 2004 until April 2005, Mr. Baird was our Vice President of Finance and Strategic Planning. From January 2002 until February

2004, Mr. Baird was our Senior Director of Finance and Strategic Planning. From August 1999 to January 2002, Mr. Baird worked at L.E.K. Consulting, a strategy consulting firm, most recently as an engagement manager. Mr. Baird received an M.B.A. in finance from The Wharton Business School and a B.S. from Georgetown University.

John Babiak, Ph.D. has been our Senior Vice President of Drug Discovery Technologies since September 2001. From March 1999 to September 2001, Dr. Babiak was Vice President of Technology at Pharmacopeia, a biopharmaceutical company. From January 1993 to March 1999, Dr. Babiak was Director of Robotics and High Throughput Screening at Wyeth-Ayerst Research, the pharmaceutical research unit of American Home Products Corporation, a pharmaceutical and health care products company. Dr. Babiak received his S.B. in physics from the Massachusetts Institute of Technology and his Ph.D. in biophysics from the University of California at Berkeley.

Mark E. Boulding has been our Senior Vice President and General Counsel and Secretary since April 2002. From May 2000 to April 2002, Mr. Boulding was the General Counsel, Executive Vice President and Secretary of MedicaLogic/ Medscape, Inc., a provider of digital health records software and healthcare information. From June 1999 to May 2000, Mr. Boulding was the General Counsel, Vice President and Secretary of Medscape, Inc., a provider of online health information and education. Prior to joining Medscape, Mr. Boulding was a partner in two Washington, D.C.-based law firms. Mr. Boulding received his J.D. from the University of Michigan and his B.A. from Yale College.

Michael Schmertzler has served as a member of our board of directors since August 2001 and as our Chairman of the Board since November 2004. Since 2001, Mr. Schmertzler has been a Managing Director of Aries Advisors, LLC, the sub-advisor to Credit Suisse First Boston Equity Partners, L.P., a private equity fund, and the Chair of the investment committee. From 1997 to 2001, Mr. Schmertzler was Co-Head of United States and Canadian Private Equity at Credit Suisse First Boston, an investment banking company. Prior to 1997, Mr. Schmertzler held various management positions with Morgan Stanley and its affiliates, including President of Morgan Stanley Leveraged Capital Funds, and was Managing Director and Chief Financial Officer of Lehman Brothers Kuhn Loeb, an investment banking firm. Mr. Schmertzler is also a director of Cytokinetics, Incorporated and, since 1978, has been an Adjunct Professor at Yale University. Mr. Schmertzler received a B.A. from Yale College in Molecular Biophysics and Biochemistry, History and City Planning and an M.B.A. from the Harvard Business School.

Harvey Berger, M.D. has served as a member of our board of directors since September 2000. Dr. Berger is the principal founder and a director of ARIAD Pharmaceuticals, Inc., a biotechnology company. He has served as ARIAD's Chairman of the Board and Chief Executive Officer since April 1991, and served as ARIAD's President from April 1991 to September 2003 and from December 2004 to present. From 1986 to 1991, Dr. Berger held a series of senior management positions at Centocor, Inc., a biotechnology company, including Executive Vice President and President, Research and Development Division. He also has held senior academic and administrative appointments at Emory University, Yale University and the University of Pennsylvania and was an Established Investigator of the American Heart Association, Inc. Dr. Berger received his A.B. degree in Biology from Colgate University and his M.D. degree from Yale University School of Medicine and did further medical and research training at the Massachusetts General Hospital and Yale-New Haven Hospital.

Axel Bolte has served as a member of our board of directors since December 2003. Since March 2003, Mr. Bolte has served as investment advisor at HBM Partners AG, a provider of investment advisory services in the life sciences industry. From March 2001 to February 2003, Mr. Bolte was an investment manager of NMT New Medical Technologies AG, a Swiss venture capital company focused on life sciences. Prior to joining NMT New Medical Technologies AG, Mr. Bolte served as a scientist at Serono SA, a biotechnology company. He currently serves on the board of directors of Newron Pharmaceuticals, SpA and Nabriva Therapeutics Forschungs GmbH, two privately held biotechnology companies. Mr. Bolte received his M.B.A from the University of St. Gallen, Switzerland and his degree in biochemistry at the Swiss Federal Institute of Technology, Zurich, Switzerland.

Søren Carlsen, Ph.D. has served as a member of our board of directors since August 2001. Dr. Carlsen has been managing partner of Novo Ventures, the venture capital division of Novo A/ S, an investment company in the life sciences industry, since May 2000. From August 1979 until May 2000, Dr. Carlsen served in various positions with Novo Nordisk A/ S, a pharmaceutical products company, including as Corporate Vice President and Chief Science Officer since 1994. Dr. Carlsen currently serves on the board of directors of various private biotechnology companies and is the chairman of the Association of Biotechnology Industries in Denmark. Dr. Carlsen received his M.Sc. in Biochemistry from the Technical University of Denmark. Dr. Carlsen has informed us that he intends to resign from our board immediately prior to the closing of this offering.

Carl Goldfischer, M.D. has served as a member of our board of directors since March 2002. Since July 2001, Dr. Goldfischer has been a Managing Director of Bay City Capital LLC, a merchant bank and management advisory firm which invests in life sciences companies, and serves on Bay City Capital's board of directors and executive committee. Dr. Goldfischer joined Bay City Capital as an Executive-in-Residence in January 2001. From May 1996 to July 2000 Dr. Goldfischer was the Vice President, Finance and Chief Financial Officer of ImClone Systems Incorporated, a biopharmaceutical company. Dr. Goldfischer is also a director of Diametrics Medical, Inc. and NeoRx Corporation and a member of the board of trustees of Sarah Lawrence College. Dr. Goldfischer received his M.D. degree from Albert Einstein College of Medicine in 1988, and served as a resident in radiation oncology at Montefiore Hospital of the Albert Einstein College of Medicine until 1991.

Allan Jacobson, Ph.D. is a co-founder of our company and has served as a member of our board of directors since our inception in 1998. Dr. Jacobson has been the Chairman of the Department of Molecular Genetics and Microbiology at the University of Massachusetts Medical School since 1994. In 1992, Dr Jacobson co-founded Applied bioTechnology, Inc., a biotechnology company, and served as its chairman until its sale in 1991. From 1987 to 1990, Dr. Jacobson served as special limited partner at Euclid Partners, a venture capital firm. Dr. Jacobson received his Ph.D. from Brandeis University in 1971. Dr. Jacobson has informed us that he intends to resign from our board immediately prior to the closing of this offering. Dr. Jacobson will continue to serve on our scientific advisory board following this offering.

Michael Kranda has been a member of our board of directors since December 2003. Since September 2003, Mr. Kranda has been director of biotechnology venture investments at Vulcan Capital, the private investment group of Vulcan Inc. From July 1996 to July 2002, Mr. Kranda served as chief executive officer at Oxford GlycoSciences, a biotechnology company. Prior to joining Oxford GlycoSciences, Mr. Kranda was President and Chief Operating Officer at Immunex Corporation (now Amgen), a biopharmaceutical company. Mr. Kranda also serves on the board of Cumbre Pharmaceuticals, BiPar Sciences, Nura, Inc., Raven Biotechnologies and the Washington State Biotechnology Business Association. Mr. Kranda received his B.A. and M.B.A from the University of Washington School of Business.

David P. Southwell has been a member of our board of directors since December 2005. Since October 1995, Mr. Southwell has been the Executive Vice President and Chief Financial Officer of Sepracor Inc., a pharmaceutical company. From July 1994 until October 1995 Mr. Southwell served as Sepracor's Senior Vice President and Chief Financial Officer. From August 1988 until July 1994, Mr. Southwell was associated with Lehman Brothers Inc., a securities firm, in various positions with the investment banking division, most recently in the position of Vice President. Mr. Southwell is a director of BioSphere Medical, Inc.

Board Composition and Election of Directors

Our board of directors is currently authorized to have, and we currently have, nine members. In accordance with the terms of our certificate of incorporation and bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be Mr. Bolte, Dr. Goldfischer and Mr. Kranda, and their term will expire at the annual meeting of stockholders to be held in 2007;

- the class II directors will be Dr. Berger and Mr. Schmertzler, and their term will expire at the annual meeting of stockholders to be held in 2008; and
- the class III directors will be Dr. Peltz and Mr. Southwell, and their term will expire at the annual meeting of stockholders to be held in 2009.

Our directors may be removed only for cause by the affirmative vote of the holders of 75% or more of our voting stock. Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. The composition of each committee will be effective upon the closing of this offering.

Audit Committee

The members of our audit committee are Mr. Southwell, Dr. Goldfischer and Mr. Kranda. Our audit committee assists our board of directors in its oversight of the integrity of our financial statements, our independent registered public accounting firm's qualifications and independence and the performance of our independent registered public accounting firm.

Upon the closing of this offering, our audit committee's responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of certain reports from our independent registered public accounting firm;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our independent registered public accounting firm and management; and
- preparing the audit committee report required by Securities and Exchange Commission rules.

All audit and non-audit services to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Mr. Southwell is our audit committee financial expert and Dr. Goldfischer is the chair of the committee. We believe that the composition of our audit committee meets the requirements for independence under the current Nasdaq National Market and Securities and Exchange Commission rules and regulations.

Compensation Committee

Dr. Berger, Mr. Bolte and Mr. Schmertzler are the members of our compensation committee. Dr. Berger is the chair of the committee. Our compensation committee assists our board of directors in the discharge of its responsibilities relating to the compensation of our executive officers.

Our compensation committee's responsibilities include:

- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our chief executive officer;
- overseeing the evaluation of performance of our senior executives;
- overseeing and administering, and making recommendations to our board of directors with respect to, our cash and equity incentive plans; and
- reviewing and making recommendations to the board of directors with respect to director compensation.

Nominating and Corporate Governance Committee

Mr. Southwell, Dr. Goldfischer and Mr. Schmertzler are the members of our nominating and corporate governance committee. Mr. Southwell is the chair of the committee.

Our nominating and corporate governance committee's responsibilities include:

- recommending to our board of directors the persons to be nominated for election as directors and to each of the board of director's committees;
- overseeing an annual evaluation of management succession planning;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing a periodic self-evaluation of our board of directors.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee has ever been our employee.

Director Compensation

In March 2005, our board of directors approved a compensation program pursuant to which we will pay each of our non-employee directors an annual retainer of 5,500 stock options for service as a director. In addition, under this program, each independent director, upon appointment to the Board of Directors, will receive a one time grant of 15,000 stock options. We will reimburse each non-employee member of our board of directors for out-of-pocket expenses incurred in connection with attending our board and committee meetings.

Executive Compensation

The following summary compensation table sets forth the total compensation paid or accrued for the year ended December 31, 2005 to our chief executive officer and our four other most highly compensated executive officers who were serving as executive officers on December 31, 2005 and whose total annual compensation

exceeded $100,000 for the year ended December 31, 2005. We refer to these officers as our “named executive officers.”

Summary Compensation Table

Name and Principal Position	Year	Annual Compensation		Long-Term Compensation	All Other Compensation
		Salary	Bonus	Shares Underlying Options (#)	
Stuart W. Peltz, Ph.D. President, Chief Executive Officer and Director	2005	$346,500	$ 83,716(1)	711,720(2)	—
William D. Ju, M.D. Chief Operating Officer	2005	$277,160	$ 50,107(3)	84,814(4)	—
Langdon Miller, M.D. Chief Medical Officer	2005	$331,800	$ 80,327(5)	131,040(6)	$ 50,890(7)
John Babiak, Ph.D. Senior Vice President, Drug Discovery Technologies	2005	$240,240	$ 43,304(8)	95,090(9)	—
Mark E. Boulding Senior Vice President and General Counsel	2005	$250,120	$ 45,084(10)	97,290(11)	—

(1) Includes $42,099 that was paid in March 2006 as part of Dr. Peltz’s 2005 bonus.
(2) Includes options to purchase 16,410 shares of common stock granted in March 2006 as part of Dr. Peltz’s 2005 bonus.
(3) Includes $24,944 that was paid in March 2006 as part of Dr. Ju’s 2005 bonus.
(4) Includes options to purchase 12,150 shares of common stock granted in March 2006 as part of Dr. Ju’s 2005 bonus.
(5) Includes $40,313 that was paid in March 2006 as part of Dr. Miller’s 2005 bonus.
(6) Includes options to purchase 16,410 shares of common stock granted in March 2006 as part of Dr. Miller’s 2005 bonus.
(7) Represents the principal amount of and applicable interest on a loan made by us to Dr. Miller which was forgiven in 2005.
(8) Includes $21,621 that was paid in March 2006 as part of Dr. Babiak’s 2005 bonus.
(9) Includes options to purchase 12,150 shares of common stock granted in March 2006 as part of Dr. Babiak’s 2005 bonus.
(10) Includes $22,510 that was paid in March 2006 as part of Mr. Boulding’s 2005 bonus.
(11) Includes options to purchase 12,150 shares of common stock granted in March 2006 as part of Mr. Boulding’s 2005 bonus.

Stock Option Grants

The following table contains information regarding grants of stock options to purchase shares of our common stock to our named executive officers during the year ended December 31, 2005.

Amounts in the following table represent potential realizable gains that could be achieved for the options if exercised at the end of the option term. The 5% and 10% assumed annual rates of compounded stock price appreciation are calculated based on the requirements of the Securities and Exchange Commission and do not represent an estimate or projection of our future common stock prices. These amounts represent certain assumed rates of appreciation in the value of our common stock from the fair market value on the date of grant. Actual gains, if any, on stock option exercises depend on the future performance of the common stock and overall stock market conditions. The amounts reflected in the following table may not necessarily be achieved.

Option Grants in Last Fiscal Year

Name	Number of Securities Underlying Options Granted (#)	Percentage of Total Options Granted to Employees in Fiscal Year	Exercise Price Per Share	Expiration Date	Potential Realizable Value of Assumed Annual Rates of Stock Price Appreciation for Option Term(1)	
					5% ($)	10% ($)
Stuart W. Peltz, Ph.D.	17,320	1%	$ 1.89	5/24/2015		
	677,990	32	1.89	11/5/2014		
William D. Ju, M.D.	12,830	1	1.89	5/24/2015		
	4	*	1.89	6/14/2014		
	59,830	3	1.89	11/5/2014		
Langdon Miller, M.D.	17,320	1	1.89	5/24/2015		
	97,310	5	1.89	11/5/2014		
John Babiak, Ph.D.	12,830	1	1.89	5/24/2015		
	70,110	3	1.89	11/5/2014		
Mark E. Boulding	12,830	1	1.89	5/24/2015		
	72,310	3	1.89	11/5/2014		

* Less than one percent.

(1) The dollar amounts under these columns are the result of calculations at rates set by the Securities and Exchange Commission and, therefore, are not intended to forecast possible future appreciation, if any, in the price of the underlying common stock. The potential realizable values are calculated using the assumed initial public offering price of $ per share and assuming that the market price appreciates from this price at the indicated rate for the entire term of each option and that each option is exercised and sold on the last day of its term at the assumed appreciated price.

Option Exercises and Year-End Option Values

The following table provides information about the number of shares issued upon option exercises by our named executive officers during the year ended December 31, 2005, and the value realized by our named executive officers. The table also provides information about the number and value of shares underlying options held by our named executive officers at December 31, 2005. There was no public trading market for our common stock as of December 31, 2005. Accordingly, as permitted by the rules of the Securities and Exchange Commission, we have calculated the value of unexercised in-the-money options at fiscal year-end assuming that the fair market value of our common stock as of December 31, 2005 was equal to the assumed initial public offering price of $ per share, less the aggregate exercise price.

Aggregated Option Exercises in Last Fiscal Year and Fiscal Year-End Option Values

Name	Shares Acquired on Exercise (#)	Value Realized	Number of Securities Underlying Unexercised Options at December 31, 2005		Value of Unexercised In-the-Money Options at December 31, 2005	
			Exercisable	Unexercisable	Exercisable	Unexercisable
Stuart W. Peltz, Ph.D.	—	—	592,756	102,571		
William D. Ju, M.D.	—	—	34,338	38,327		
Langdon Miller, M.D.	—	—	55,773	58,862		
John Babiak, Ph.D.	—	—	47,122	35,822		
Mark E. Boulding	—	—	48,661	36,483		

Employment Agreements

Stuart W. Peltz, Ph.D. Pursuant to an employment agreement effective August 1, 2002, we employ Dr. Peltz as our president and chief executive officer. Under this agreement, Dr. Peltz is entitled to an annual base salary of at least $280,000. Adjustments to his base salary are in the discretion of our board of directors. We have agreed not to reduce his base salary below $280,000 unless the reduction is in connection with a general reduction in compensation of our senior executives. The agreement provides that Dr. Peltz is eligible to participate in any executive bonus plans established by the board from time to time.

The agreement will continue for successive one-year terms until either Dr. Peltz or we provide written notice of termination to the other in accordance with the terms of the agreement. Upon the termination of his employment by us other than for cause, or by him for good reason, including a change in our control where the successor company does not assume our obligations to him, Dr. Peltz has the right to receive a severance payment in an amount equal to 18 times his monthly base salary then in effect, payable in accordance with our regular payroll schedule. In addition, Dr. Peltz is entitled to the continuation of benefits for a comparable period as a result of any such termination. Dr. Peltz is not entitled to severance payments if we terminate him for cause or if he resigns without good reason. Dr. Peltz is bound by non-disclosure, inventions and non-competition covenants that prohibit him from competing with us during the term of his employment and for one year after termination of employment.

Other Named Executive Officers. We entered into an employment agreement with Langdon Miller, M.D. in December 2004, under which he is employed as our chief medical officer. Under this agreement, Dr. Miller is entitled to an annual base salary of at least $331,800. In addition, we agreed to provide Dr. Miller with a loan of $50,000 per year during a three-year period beginning on his start date, with the remaining loan, funded on the first and second anniversaries of his start date. We agreed to forgive each loan on the anniversary of the date on which it was made as long as Dr. Miller remained an employee on that date.

Under our employment agreement with William D. Ju, M.D., he is employed as our chief operating officer, at an annual base salary of at least $277,160. Under our employment agreement with John Babiak, Ph.D., he is employed as our senior vice president, discovery technologies, at an annual base salary of

at least $240,240. Under our employment agreement with Mark E. Boulding, he is employed as our senior vice president and general counsel, at an annual base salary of at least $250,120.

Our executive employment agreements with Drs. Ju, Miller and Babiak and Mr. Boulding each provide that any increase to the executive's base salary is in the sole discretion of the compensation committee of our board of directors. In addition to their base salary, we have agreed to pay each executive a discretionary bonus annually if, in the judgment of the compensation committee, the qualifying criteria established by the committee for payment of a bonus have been met. Pursuant to the agreements, each executive is entitled also to such other benefits as we generally provide our senior executives. In addition, one half of any outstanding unvested stock options granted to each executive will vest immediately upon a change in our control or other specified corporate change, and the remainder will vest proportionately according to their terms.

Each executive employment agreement has an initial term that expires December 15, 2007, and will continue thereafter for successive one-year periods until we provide the executive with written notice in accordance with its terms. Should we or our successor terminate an executive's employment other than for good cause within two years following certain corporate changes, the executive has the right to receive a lump-sum severance payment in an amount equal to 12 times his monthly base salary in effect as of the date of the corporate change or as of the date of termination, whichever is greater, and any outstanding unvested stock options held by him will vest. Any reduction in an executive's base salary or significant reduction in his duties following such a corporate change entitles the executive to immediate vesting of outstanding stock options and severance payment. Each executive is not otherwise entitled to accelerated vesting or severance payment under the agreements in cases where no such corporate change occurs, where we terminate his employment for good cause or where he resigns. Each executive is bound by non-disclosure, inventions, non-solicitation and non-competition covenants that prohibit him from competing with us during the term of his employment and for 12 months after termination of employment.

Stock Option and Other Compensation Plans

1998 Employee, Director and Consultant Stock Option Plan

Our 1998 employee, director and consultant stock option plan, as amended and restated from time to time, was adopted by our board of directors and approved by our stockholders. The plan provides for the grant of incentive stock options and non-statutory stock options. A maximum of 2,426,008 shares of common stock are authorized for issuance under our 1998 stock option plan.

In accordance with the terms of the 1998 stock option plan, our board of directors has authorized our compensation committee to administer the plan.

Under our 1998 stock option plan, if a merger or other reorganization event occurs, our board of directors, in its discretion, shall either:

- provide that the outstanding options under the 1998 stock option plan be assumed or substituted by the successor corporation;
- upon written notice to optionees, provide that all unexercised options will terminate, unless exercised, immediately prior to the consummation of such transaction; or
- provide that all or any of our outstanding options will terminate in exchange for a cash payment equal to their value.

As of March 15, 2006, there were options to purchase 2,340,715 shares of common stock outstanding under the 1998 stock option plan and options to purchase 11,828 shares of common stock had been exercised. After the effective date of the 2006 equity plan described below, we will grant no further stock options under the 1998 stock option plan.

2006 Equity and Long Term Incentive Plan

Our 2006 equity plan was adopted by our board of directors on , 2006 and approved by our stockholders on , 2006. The 2006 equity plan will become effective on the date that the registration statement of which this prospectus forms a part is declared effective. The 2006 equity plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards and other stock unit awards. Upon effectiveness, shares of common stock will be reserved for issuance under the 2006 equity plan.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under our 2006 equity plan. Incentive stock options may only be granted to our employees. The maximum number of shares of common stock with respect to which awards may be granted to any participant under the plan is per calendar year.

In accordance with the terms of the 2006 equity plan, our board of directors has authorized our compensation committee to administer the plan. Our compensation committee selects the recipients of awards and determines:

- the number of shares of common stock covered by options and the dates upon which the options become exercisable;
- the exercise price of options; provided, however, that the exercise price shall not be less than 100% of fair market value of the stock on the date of grant;
- the duration of options, provided that no option shall have a term in excess of 10 years;
- the method of payment of the exercise price; and
- the number of shares of common stock subject to any restricted stock or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price.

If our board of directors delegates authority to an executive officer, the executive officer has the power to make awards to all of our employees, except to executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards, and the maximum number of shares subject to awards that such executive officer may make.

If a merger or other reorganization event occurs, our board of directors shall provide that all of our outstanding options are to be assumed or substituted by the successor corporation. If the merger or reorganization event also constitutes a change in control event as defined under our 2006 equity plan, the assumed or substituted options will become immediately exercisable in full if on or prior to the 18-month anniversary of the reorganization event an option holder's employment with us or our succeeding corporation is terminated by the option holder for good reason or is terminated by us or the succeeding corporation without cause, each as defined in our 2006 equity plan. In the event the succeeding corporation does not agree to assume, or substitute for, outstanding options, then our board of directors shall provide that all unexercised options will become exercisable in full prior to the completion of the event and that these options will terminate immediately prior to the completion of the merger or other reorganization event if not previously exercised. Our board of directors may also provide for a cash out of the value of any outstanding options. In addition, upon the occurrence of a change in control event that does not also constitute a reorganization event under our 2006 equity plan, each option will continue to vest according to its original vesting schedule, except that an option will become immediately exercisable in full if on or prior to the 18-month anniversary of the reorganization event an option holder's employment with us or our succeeding corporation is terminated by the option holder for good reason or is terminated by us or our succeeding corporation without cause.

No award may be granted under the 2006 equity plan after , 2016, but the vesting and effectiveness of awards granted before that date may extend beyond that date. Our board of directors may amend, suspend or terminate the 2006 equity plan at any time, except that stockholder approval will be required for any revision that would materially increase the number of shares reserved for issuance, expand the

types of awards available under the plan, materially modify plan eligibility requirements, extend the term of the plan or materially modify the method of determining the exercise price of options granted under the plan, or otherwise as required to comply with applicable law or stock market requirements.

2006 Employee Stock Purchase Plan

On , 2006, our board of directors approved our 2006 employee stock purchase plan. The 2006 employee stock purchase plan, which was approved by stockholders in 2006, became effective on . The plan provides for the issuance of up to shares of our common stock to participating employees.

All of our employees, including directors who are employees, and all employees of any participating subsidiaries:

- whose customary employment is more than 20 hours per week for more than five months in a calendar year;
- who were employed by us for at least 90 days prior to enrolling, other than in connection with the initial plan period; and
- who are employed on the first day of a designated payroll deduction offering period

are eligible to participate in the 2006 employee stock purchase plan.

Employees who would immediately after the grant of an option under the 2006 employee stock purchase plan own 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries are not eligible to participate in the plan.

We will make one or more offerings to our employees to purchase stock under the 2006 employee stock purchase plan. Offerings will begin on each April 1 and October 1, except that our first offering will begin on the date on which trading of our common stock commences on the Nasdaq National Market in connection with this offering. Each offering commencement date, except the first offering, will begin a six-month period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors may, in its discretion, choose a different offering period for each subsequent offering.

On the first day of an offering period, we will grant to each eligible employee who has elected to participate in the 2006 employee stock purchase plan an option to purchase shares of our common stock as follows: the employee may authorize up to 10% of his or her compensation (as defined in the plan) to be deducted by us during the offering period. On the last day of the offering period, the employee is deemed to have exercised the option, at the option exercise price, to the extent of accumulated payroll deductions. Under the terms of the 2006 employee stock purchase plan, the option exercise price is an amount equal to 85% of the lower of the closing price of our common stock on the first day or the last day of the offering period. For purposes of the first offering period under the 2006 employee stock purchase plan, the closing price of our common stock on the first day of such period is deemed to equal the initial public offering price per share in this offering.

In no event may an employee be granted an option under the plan which permits his rights to purchase stock under the plan (or any other employee stock purchase plan of ours or our subsidiaries) to accrue at a rate which exceeds $25,000 of our common stock at fair market value for each calendar year in which the option is outstanding at any time.

An employee who is not a participant on the last day of the offering period is not entitled to exercise any option, and the employee’s accumulated payroll deductions will be refunded. An employee’s rights under the 2006 employee stock purchase plan terminate upon voluntary withdrawal from the purchase plan at any time, or when the employee ceases employment for any reason, except that upon termination of employment because of death, the balance in the employee’s account will be paid to the employee’s beneficiary.

Because participation in the 2006 employee stock purchase plan is voluntary, we cannot now determine the number of shares of our common stock to be purchased by any particular current executive officer, by all current executive officers as a group or by non-executive employees as a group.

Limitation of Liability and Indemnification of Officers and Directors

Our certificate of incorporation that will be in effect upon the closing of this offering limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law. Our certificate of incorporation provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of their duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for voting or assenting to unlawful payments of dividends or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act or failure to act, or any cause of action, suit or claim that would accrue or arise prior to any amendment or repeal or adoption of an inconsistent provision. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Since January 1, 2003, we have engaged in the following transactions with our directors, executive officers and holders of more than 5% of our voting securities on an as converted to common stock basis, and affiliates of our directors, executive officers and holders of more than 5% of our voting securities. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Issuance of Series E and Series E-2 Convertible Preferred Stock

In December 2003 and in April and June 2004, we issued an aggregate of 125,740,607 shares of our Series E convertible preferred stock at a price of approximately $0.40 per share for total cash proceeds to us of approximately $50.0 million before transaction expenses. In September and October 2005, we issued an aggregate of 3,670,138 shares of our Series E-2 convertible preferred stock at a price of $7.26 per share for total cash proceeds to us of approximately $26.6 million before transaction expenses.

The following table sets forth the number of shares of Series E convertible preferred stock and Series E-2 convertible preferred stock sold to our 5% stockholders and directors and their affiliates in these financings. The shares of Series E convertible preferred stock referred to in the table will convert automatically into an aggregate of 5,466,386 shares of our common stock upon the closing of this offering. The shares of Series E-2 convertible preferred stock referred to in the table will convert automatically into an aggregate of 2,803,265 shares of our common stock upon the closing of this offering.

Name	Number of Shares of Series E Preferred Stock	Number of Shares of Series E-2 Preferred Stock
Entities affiliated with Credit Suisse(1)	35,699,539	890,854
HBM BioVentures (Cayman) Ltd.(2)	18,315,568	824,187
Vulcan Capital Venture Holdings Inc.(3)	16,708,349	330,650
Entities affiliated with Delphi Ventures(4)	13,493,914	275,482
Entities affiliated with Bay City Capital(5)	10,059,249	206,610
Novo A/S(6)	5,532,586	275,482
Total	99,806,205	2,803,265

(1) Includes 27,879,539 shares of Series E convertible preferred stock and 695,712 shares of Series E-2 convertible preferred stock issued to Credit Suisse First Boston Equity Partners, L.P.; 7,793,048 shares of Series E convertible preferred stock and 194,469 shares of Series E-2 convertible preferred stock issued to Credit Suisse First Boston Equity Partners (Bermuda), L.P.; and 26,952 shares of Series E convertible preferred stock and 673 shares of Series E-2 convertible preferred stock issued to Credit Suisse First Boston U.S. Executive Advisors, L.P. Mr. Schmertzler, one of our directors, is a Managing Director of Aries Advisors, LLC, an affiliate of Credit Suisse.

(2) Mr. Bolte, one of our directors, is an employee of HBM Partners AG. HBM Partners AG acts as an investment advisor to HBM BioVentures (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM BioVentures (Cayman) Ltd. Neither HBM Partners AG nor Mr. Bolte have voting or investment power over the shares held by HBM BioVentures (Cayman) Ltd.

(3) Mr. Kranda, one of our directors, is director of biotechnology venture investments at Vulcan Inc.

(4) Includes 13,349,165 shares of Series E convertible preferred stock and 272,527 shares of Series E-2 convertible preferred stock issued to Delphi Ventures V, L.P.; and 144,749 shares of Series E convertible preferred stock and 2,955 shares of Series E-2 convertible preferred stock issued to Delphi BioInvestments V, L.P.

(5) Includes 9,637,670 shares of Series E convertible preferred stock and 197,952 shares of Series E-2 convertible preferred stock issued to The Bay City Capital Fund III, L.P.; and 421,579 shares of Series E convertible preferred stock and 8,658 shares of Series E-2 convertible preferred stock issued to The Bay

City Capital Fund III Co-Investment Fund, L.P. Dr. Goldfischer, one of our directors, is a Managing Director of Bay City Capital LLC.

(6) Dr. Carlsen, one of our directors, is managing partner of Novo Ventures, an affiliate of Novo A/S.

Certain Relationships

Registration Rights

Pursuant to an investor rights agreement among holders of our Series A, Series B, Series C, Series D, Series E and Series E-2 convertible preferred stock and us, we granted registration rights to all such holders. Entities affiliated with Credit Suisse, HBM BioVentures (Cayman) Ltd., Vulcan Capital Venture Holdings Inc., Delphi Ventures, Bay City Capital LLC, holders of 5% or more of our voting securities, and their affiliates are each a party to this investor rights agreement. See “Description of Capital Stock—Registration Rights.”

Loan to Executive Officer

In connection with his initial offer of employment, we extended a series of interest-bearing loans in the aggregate principal amount of $150,000 to Dr. Langdon Miller, our Chief Medical Officer. As of December 31, 2005, in accordance with Dr. Miller’s employment terms, we have forgiven an aggregate of $100,000 in principal amount of these loans. We forgave the final $50,000 loan to Dr. Miller in the first quarter of 2006.

Director Compensation

Please see “Management—Director Compensation” for a discussion of options granted and other compensation to our non-employee directors.

Executive Compensation and Employment Agreements

Please see “Management—Executive Compensation” and “—Stock Options” for additional information on compensation of our executive officers. Information regarding employment agreements with our executive officers is set forth under “Management—Employment Agreements.”

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock, as of March 15, 2006, by:

- each of our directors;
- each of our named executive officers;
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock; and
- all of our directors and executive officers as a group.

The column entitled "Percentage of Shares Beneficially Owned— Before Offering" is based on a total of 13,516,611 shares of our common stock outstanding on March 15, 2006, assuming conversion of all outstanding shares of our preferred stock into common stock upon the closing of this offering. The column entitled "Percentage of Shares Beneficially Owned— After Offering" is based on shares of common stock to be outstanding after this offering, including the shares that we are selling in this offering, but not including any shares issuable upon exercise of warrants or options.

For purposes of the table below, we deem shares of common stock subject to options or warrants that are currently exercisable or exercisable within 60 days of March 15, 2006 to be outstanding and to be beneficially owned by the person holding the options or warrants for the purpose of computing the percentage ownership of that person but we do not treat them as outstanding for the purpose of computing the percentage ownership of any other person. Except as otherwise noted, the persons or entities in this table have sole voting and investing power with respect to all of the shares of common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the street address of the beneficial owner is c/o PTC Therapeutics, Inc., 100 Corporate Court, South Plainfield, New Jersey 07080-2449.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
5% Stockholders			
Entities affiliated with Credit Suisse(1) Eleven Madison Avenue, 16th Floor New York, NY 10010	3,435,467	25.2%	
HBM BioVentures (Cayman) Ltd.(2) Centennial Towers, 3rd Floor 2454 West Bay Road Grand Cayman, Cayman Islands	2,017,840	14.9	
Entities affiliated with Vulcan Capital Venture Holdings Inc.(3) 505 Fifth Avenue South, Suite 900 Seattle, WA 98104	1,904,527	14.1	
Entities affiliated with Delphi Ventures(4) 3000 Sand Hill Road, Building 1, Suite 135, Menlo Park, CA 94025	1,169,330	8.7	
Entities affiliated with the Bay City Capital Fund(5) 750 Battery Street, Suite 400 San Francisco, CA 94111	995,669	7.4	
Novo A/S(6) Krogshoejvej 41 2880 Bagsvaerd, Denmark	697,559	5.2	

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
Executive Officers and Directors			
Stuart W. Peltz, Ph.D.(7)	624,445	4.4	
William D. Ju, M.D.(8)	47,173	*	
Langdon Miller, M.D.(9)	75,151	*	
John Babiak, Ph.D.(10)	59,420	*	
Mark E. Boulding(11)	61,143	*	
Michael Schmertzler(12)	2,751	*	
Harvey Berger, M.D.(13)	460	*	
Axel Bolte(14)	—	—	
Søren Carlsen, Ph.D.(15)	1	*	
Carl Goldfischer, M.D.(16)	1	*	
Allan Jacobson, Ph.D.(17)	156,118	1.1	
Michael Kranda	—	—	
David P. Southwell	1,250	*	
All directors and executive officers as a group (14 persons)(18)	1,073,498	7.4	

* Less than one percent.

(1) Consists of 2,662,259 shares held by Credit Suisse First Boston Equity Partners, L.P.; 744,169 shares held by Credit Suisse First Boston Equity Partners (Bermuda), L.P.; 2,573 shares held by Credit Suisse First Boston U.S. Executive Advisors, L.P.; 24,800 shares held by EMA Private Equity Fund 1999, L.P.; and 1,666 shares held by Credit Suisse First Boston Finders & Screeners, L.P. Mr. Schmertzler, a member of our board of directors, is a Managing Director of Aries Advisors, LLC, the sub-advisor to Credit Suisse First Boston Equity Partners, L.P., who disclaims beneficial ownership of the shares held by entities affiliated with Credit Suisse except to the extent of any pecuniary interest therein.

(2) Consists of 2,017,840 shares held by HBM BioVentures (Cayman) Ltd. The board of directors of HBM BioVentures (Cayman) Ltd. has sole voting and investment power with respect to the shares by held by such entity and acts by majority vote. The board of directors of HBM BioVentures (Cayman) Ltd. is comprised of John Arnold, Colin Shaw, Richard Coles, Dr. Andreas Wicki and John Urquhart, none of whom has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of the shares held by HBM except to the extent of any pecuniary interest therein. Mr. Bolte, a member of our board of directors, is an employee of HBM Partners AG. HBM Partners AG acts as an investment advisor to HBM Partners (Cayman) Ltd. HBM Partners (Cayman) Ltd. provides investment management services to HBM BioVentures (Cayman) Ltd. Neither HBM Partners AG nor Mr. Bolte have voting or investment power over the shares held by HBM BioVentures (Cayman) Ltd.

(3) Consists of 330,650 shares held by Vulcan Capital Venture Holdings Inc. and 1,573,877 shares held by Vulcan Ventures Inc. Mr. Kranda, a member of our board of directors, is a Managing Director of Vulcan Inc. and is responsible for its biotech venture investments. Vulcan Capital Venture Holdings Inc. and Vulcan Ventures Inc. are wholly-owned by the sole stockholder of Vulcan Inc.

(4) Consists of 1,156,787 shares held by Delphi Ventures V, L.P. and 12,543 shares held by Delphi BioInvestments V, L.P.

(5) Consists of 953,944 shares held by The Bay City Capital Fund III, L.P. and 41,725 shares held by The Bay City Capital Fund III Co-Investment Fund, L.P. Dr. Goldfischer, a member of our board of directors, is a Managing Director of Bay City Capital LLC, and serves on Bay City Capital's board of managers and investment committee. Bay City Capital LLC is the manager of the general partner of the above mentioned funds. Dr. Goldfischer disclaims beneficial ownership of the shares held by Bay City except to the extent of any pecuniary interest therein.

(6) Novo A/S is a Danish private limited liability company fully owned by the Novo Nordisk Foundation. Dr. Carlsen, a member of our board of directors and is Managing Partner of Novo A/ S. Dr. Carlsen disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest arising as a result of his engagement with Novo A/ S.
(7) Consists of 624,417 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006 and 28 shares of common stock.
(8) Consists of 47,173 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006.
(9) Consists of 75,151 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006.
(10) Consists of 59,420 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006.
(11) Consists of 61,143 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006.
(12) Consists of 2,751 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006. Mr. Schmertzler disclaims beneficial ownership of the shares held by Credit Suisse First Boston except to the extent of his pecuniary interest therein. See footnote 1.
(13) Consists of 460 shares issuable upon exercise of stock options exercisable within 60 days of March 15, 2006.
(14) Mr. Bolte disclaims beneficial ownership of the shares held by HBM BioVentures (Cayman) Ltd. except to the extent of his pecuniary interest therein. See footnote 2.
(15) Dr. Carlsen disclaims beneficial ownership of the shares held by Novo A/S except to the extent of his pecuniary interest therein. See footnote 6.
(16) Dr. Goldfischer disclaims beneficial ownership of the shares held by the Bay City Capital Fund except to the extent of his pecuniary interest therein. See footnote 5.
(17) Consists of 156,093 shares issuable upon the exercise of stock options exercisable within 60 days of March 15, 2006 and 28 shares of common stock.
(18) Consists of 1,073,442 shares issuable upon the exercise of stock options exercisable within 60 days of March 15, 2006 and includes 56 shares of common stock.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws that will be in effect upon the closing of this offering. We have filed copies of these documents with the Securities and Exchange Commission as exhibits to our registration statement of which this prospectus forms a part. The description of the capital stock reflects changes to our capital structure that will occur upon the closing of this offering.

Upon the closing of this offering, our authorized capital stock will consist of shares of common stock, par value $0.001 per share, and shares of preferred stock, par value $0.001 per share, all of which preferred stock will be undesignated.

As of March 15, 2006, we had issued and outstanding:

- 11,889 shares of common stock outstanding held by 14 stockholders of record;
- 750,000 shares of Series A convertible preferred stock that are convertible into 62,500 shares of common stock;
- 187,500 shares of Series B convertible preferred stock that are convertible into 25,000 shares of common stock;
- 6,000,000 shares of Series C convertible preferred stock that are convertible into 833,325 shares of common stock;
- 13,095,769 shares of Series D convertible preferred stock that are convertible into 2,026,717 shares of common stock;
- 125,740,607 shares of Series E convertible preferred stock that are convertible into 6,887,042 shares of common stock; and
- 3,670,138 shares of Series E-2 convertible preferred stock that are convertible into 3,670,138 shares of common stock.

As of March 15, 2006, we also had outstanding:

- options to purchase 2,340,715 shares of common stock at a weighted average exercise price of $2.40 per share;
- a warrant to purchase 77,380 shares of common stock at an exercise price of $21.00 per share;
- a warrant to purchase 295,000 shares of Series C preferred stock at an exercise price of $2.50 per share;
- warrants to purchase an aggregate of 674,166 shares of Series D preferred stock at an exercise price of $3.25 per share; and
- warrants to purchase an aggregate of 994,415 shares of Series E preferred stock at an exercise price of $.397644 per share.

Upon the closing of this offering, all of the outstanding shares of our preferred stock will automatically convert into a total of 13,504,722 shares of our common stock. In addition, upon the closing of this offering and after giving effect to the automatic conversion of our preferred stock into common stock, warrants to purchase an aggregate of 277,151 shares of common stock will remain outstanding.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders

of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Warrants

As of March 15, 2006, we had outstanding a warrant to purchase 77,380 shares of common stock at an exercise price of $21.00 per share, a warrant to purchase 295,000 shares of Series C preferred stock at an exercise price of $2.50 per share, warrants to purchase an aggregate of 674,166 shares of Series D preferred stock at an exercise price of $3.25 per share and warrants to purchase an aggregate of 994,415 shares of Series E preferred stock at an exercise price of $.397644 per share.

Upon the closing of this offering, the warrant to purchase shares of Series C preferred stock will automatically convert into a warrant to purchase 40,972 shares of common stock at an exercise price of $18.00 per share, the warrants to purchase shares of Series D preferred stock will automatically convert into warrants to purchase an aggregate of 104,334 shares of common stock at an exercise price of $21.00 per share and the warrants to purchase shares of Series E preferred stock will automatically convert into warrants to purchase an aggregate of 54,465 shares of common stock at an exercise price of $7.26 per share. Accordingly, upon the closing of this offering, we will have outstanding warrants to purchase an aggregate of 277,151 shares of our common stock at a weighted average exercise price of $17.86 per share. The warrants provide for adjustments in the event of specified mergers, reorganizations, reclassifications, stock dividends, stock splits or other changes in our corporate structure. The warrants also provide for cashless exercise. The warrants expire on various dates between March 14, 2008 and April 21, 2014.

The warrant to purchase 77,380 shares of common stock contains vesting provisions. As of March 15, 2006, that warrant was vested with respect to 61,904 shares. The warrant would vest with respect to the remaining 15,476 shares if we receive marketing approval for PTC124 from the FDA or any similar regulatory authority outside the United States.

Options

As of March 15, 2006, options to purchase 2,340,715 shares of common stock at a weighted average exercise price of $2.40 per share were outstanding.

Anti-Takeover Effects of Delaware Law and our Corporate Charter Documents

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that will own 15% or more of our outstanding voting stock upon the closing of this offering.

Staggered Board

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our chairman of the board, our president or chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to the board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

Super-Majority Voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that

all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Registration Rights

Upon the closing of this offering, holders of an aggregate of shares of our common stock, including shares of common stock underlying outstanding warrants, will have the right to require us to register these shares under the Securities Act under specified circumstances.

Demand and Form S-3 Registration Rights

Beginning six months after the closing of this offering, subject to specified limitations, these stockholders may require that we register all or part of these securities for sale under the Securities Act on two occasions. In addition, these stockholders may from time to time make demand for registrations on Form S-3, a short form registration statement, when we are eligible to use this form.

Incidental Registration Rights

If we register any of our common stock, either for our own account or for the account of other securityholders, these stockholders are entitled to notice of the registration and to include their shares of common stock in the registration.

Limitations and Expenses

Other than in a demand registration, with specified exceptions, a holder's right to include shares in a registration is subject to the right of the underwriters to limit the number of shares included in the offering. All fees, costs and expenses of any demand registrations and any registrations on Form S-3 will be paid by us, and all selling expenses, including underwriting discounts and commissions, will be paid by the holders of the securities being registered.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company.

Nasdaq National Market

We have applied to have our common stock approved for quotation on The Nasdaq National Market under the symbol "PTCT."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no market for our common stock, and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of common stock, including shares issued upon exercise of outstanding options and warrants or in the public market after this offering, or the anticipation of those sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of our equity securities.

Upon the closing of this offering, we will have outstanding shares of common stock, after giving effect to the issuance of shares of common stock in this offering and the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 13,504,722 shares of our common stock and assuming no exercise of the underwriters' over-allotment option and no exercise of options or warrants outstanding as of December 31, 2005.

Of the shares to be outstanding immediately after the closing of this offering, the shares to be sold in this offering will be freely tradable without restriction under the Securities Act unless purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining shares of common stock are "restricted securities" under Rule 144. Substantially all of these restricted securities will be subject to the 180-day lock-up period described below.

After the 180-day lock-up period, these restricted securities may be sold in the public market only if registered or if they qualify for an exemption from registration under Rule 144 or 701 under the Securities Act, which exemptions are summarized below.

Rule 144

In general, under Rule 144, beginning 90 days after the date of this prospectus, a person who has beneficially owned shares of our common stock for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell within any three-month period a number of shares that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering, and
- the average weekly trading volume in our common stock on The Nasdaq National Market during the four calendar weeks preceding the date of filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us. Upon expiration of the 180-day lock-up period described below, of shares of our common stock will be eligible for sale under Rule 144, excluding shares eligible for resale under Rule 144(k) as described below. We cannot estimate the number of shares of common stock that our existing stockholders will elect to sell under Rule 144.

Rule 144(k)

Subject to the lock-up agreements described below, shares of our common stock eligible for sale under Rule 144(k) may be sold immediately upon the closing of this offering. In general, under Rule 144(k), a person may sell shares of common stock acquired from us immediately upon the closing of this offering, without regard to manner of sale, the availability of public information about us or volume limitations, if:

- the person is not our affiliate and has not been our affiliate at any time during the three months preceding the sale; and
- the person has beneficially owned the shares proposed to be sold for at least two years, including the holding period of any prior owner other than our affiliates.

Upon the expiration of the 180-day lock-up period described below, approximately shares of common stock will be eligible for sale under Rule 144(k).

Rule 701

In general, under Rule 701 of the Securities Act, any of our employees, consultants or advisors who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement is eligible to resell those shares 90 days after the effective date of this offering in reliance on Rule 144, but without compliance with the various restrictions, including the holding period, contained in Rule 144. Subject to the 180-day lock-up period described below, approximately shares of our common stock will be eligible for sale in accordance with Rule 701.

Lock-up Agreements

We expect that the holders of substantially all of our currently outstanding capital stock will agree that, without the prior written consent of Morgan Stanley, they will not, during the period ending 180 days after the date of this prospectus, subject to exceptions specified in the lock-up agreements, offer, sell, contract to sell or otherwise dispose of, directly or indirectly, or hedge our common stock or securities convertible into or exchangeable for or exercisable for our common stock, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable for our common stock. Further, these holders have agreed that, during this period, they will not make any demand for, or exercise any right with respect to, the registration of our common stock or warrants or other rights to purchase the common stock.

Registration Rights

Upon the closing of this offering, the holders of an aggregate of shares of our common stock, including shares of common stock underlying outstanding warrants, will have the right to require us to register these shares under the Securities Act under specified circumstances. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. Please see “Description of Capital Stock— Registration Rights” for additional information regarding these registration rights.

Stock Options

As of March 15, 2006, we had outstanding options to purchase 2,340,715 shares of common stock, of which options to purchase 1,545,064 shares were vested. Following this offering, we intend to file registration statements on Form S-8 under the Securities Act to register all of the shares of common stock subject to outstanding options and options and other awards issuable pursuant to our 1998 stock option plan, our 2006 equity plan and our 2006 employee stock purchase plan. Please see “Management— Stock Option and Other Compensation Plans” for additional information regarding these plans. Accordingly, shares of our common stock registered under the registration statements will be available for sale in the open market, subject to Rule 144 volume limitations applicable to affiliates, and subject to any vesting restrictions and lock-up agreements applicable to these shares.

Warrants

Upon the closing of this offering, we will have outstanding warrants to purchase an aggregate of 277,151 shares of our common stock at a weighted average exercise price of $17.86 per share. Any shares purchased pursuant to the cashless exercise features of these warrants will be freely tradable under Rule 144(k), subject to the 180-day lock-up period described above.

UNDERWRITERS

Under the terms and subject to the conditions contained in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. Incorporated, J.P. Morgan Securities Inc. and Pacific Growth Equities, LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares of common stock indicated in the table below:

Name	Number of Shares
Morgan Stanley & Co. Incorporated	
J.P. Morgan Securities Inc.	
Pacific Growth Equities, LLC	
Total	

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $ a share under the public offering price. No underwriter may allow, and no dealer may re-allow, any concession to other underwriters or to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to an aggregate of additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table. If the underwriters' over-allotment option is exercised in full, the total price to the public would be $, the total underwriters' discounts and commissions would be $ and the total proceeds to us would be $.

The following table shows the per share and total underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of our common stock.

	No Exercise	Full Exercise
Per share	$	$
Total	$	$

In addition, we estimate that the expenses of this offering payable by us, other than underwriting discounts and commissions, will be approximately $ million.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed five percent of the total number of shares of common stock offered by them.

We, all of our directors and executive officers and holders of substantially all of our outstanding stock have agreed that, without the prior written consent of Morgan Stanley & Co. Incorporated on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for our common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise.

The 180-day restricted period described in the preceding paragraph will be extended if:

- during the last 17 days of the 180-day restricted period we issue an earnings release or material news or a material event relating to our company occurs; or
- prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period,

in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

These restrictions do not apply to:

- the sale of shares to the underwriters;
- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;
- the grant of options or the issuance of shares of common stock by us pursuant to our equity plans described in this prospectus, provided that the recipient of the options or shares agrees to be subject to the restrictions described above;
- the issuance by us of shares of common stock in connection with strategic transactions, such as collaboration or license agreements, provided that the recipient of the shares agrees to be subject to the restrictions described above;
- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the closing of the offering of the shares;
- transfers by any person other than us of shares of common stock or other securities as a bona fide gift; or
- distributions other than by us of shares of common stock or other securities to limited partners or stockholders;

provided that in the case of each of the last three transactions, no filing under Section 16(a) of the Exchange Act is required or is voluntarily made in connection with the transaction, and in the case of each of the last two transactions, each donee or distributee agrees to be subject to the restrictions on transfer described above.

In order to facilitate this offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by

exercising the over-allotment option or by purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. In addition, to stabilize the price of the common stock, the underwriters may bid for, and purchase shares of common stock in the open market. Finally, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the common stock in the offering, if the syndicate repurchases previously distributed common stock in transactions to cover syndicate short positions or to stabilize the price of the common stock. Any of these activities may stabilize or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

We have applied for quotation of our common stock on the Nasdaq National Market under the symbol “PTCT.”

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

Directed Share Program

At our request, the underwriters have reserved for sale, at the initial public offering price, up to shares offered by this prospectus to directors, officers, employees and other individuals associated with us through a directed share program. The number of shares of our common stock available for sale to the general public in the offering will be reduced to the extent these persons purchase these reserved shares. Any reserved shares not purchased by these persons will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus. Recipients of reserved shares will be required to agree with the underwriters not to sell, transfer, assign, pledge or hypothecate these shares for a period of 180 days after purchasing the shares.

Pricing of the Offering

Prior to this offering, there has been no public market our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. Among the factors to be considered in determining the initial public offering price will be our future prospects and those of our industry in general, our sales, earnings and other financial operating information in recent periods, and the price-earnings ratios, price-sales ratios and market prices of securities and certain financial and operating information of companies engaged in activities similar to ours. The estimated initial public offering price range set forth on the cover page of this preliminary prospectus is subject to change as a result of market conditions and other factors.

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters, and one or more of the underwriters may distribute prospectuses electronically. The underwriters may agree to allocate a number of shares to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters that make Internet distributions on the same basis as other allocations.

LEGAL MATTERS

The validity of the common stock we are offering will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York. Ropes & Gray LLP has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

The financial statements of PTC Therapeutics, Inc. (a development-stage company) as of December 31, 2004 and 2005, and for each of the years in the three-year period ended December 31, 2005 and for the period from March 31, 1998 (inception) to December 31, 2005, have been included herein and in the registration statement in reliance upon the reports of KPMG LLP, independent registered public accounting firm, and Arthur Andersen LLP, independent accountants, appearing elsewhere herein, and upon the authority of said firms as experts in accounting and auditing.

KPMG LLP's audit report contains an explanatory paragraph that refers to KPMG LLP's audit of the adjustments that were applied to restate the cumulative statements of operations, stockholders' equity (deficit) and comprehensive loss, and cash flows for the period from March 31, 1998 (inception) to December 31, 2001, as more fully described in note 2(o) to the financial statements. However, KPMG LLP was not engaged to audit, review or apply procedures to the cumulative financial statements for the period from March 31, 1998 (inception) to December 31, 2001 other than with respect to such adjustments, and accordingly, KPMG LLP did not express an opinion or any other form of assurance on the cumulative financial statements for the period from March 31, 1998 (inception) to December 31, 2001, taken as a whole.

The cumulative statements of operations, stockholders' equity (deficit) and comprehensive loss, and cash flows for the period from March 31, 1998 (inception) to December 31, 2001 of PTC Therapeutics, Inc. (a development-stage company), included herein and in the registration statement, have been audited by Arthur Andersen LLP, our former accountants. You have no effective remedy against Arthur Andersen in connection with a material misstatement or omission in those financial statements, particularly in the event that Arthur Andersen ceases to exist as an entity or becomes insolvent as a result of proceedings against it.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract or any other document are not necessarily complete, and, in each instance, we refer you to the copy of the contract or other documents filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You may read and copy the registration statement of which this prospectus is a part at the Securities and Exchange Commission's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of the registration statement by writing to the Securities and Exchange Commission and paying a fee for the copying cost. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for more information about the operation of the Securities and Exchange Commission's public reference room. In addition, the Securities and Exchange Commission maintains an Internet website, which is located at http://www.sec.gov, that contains reports, proxy and information statements and other information regarding issuers that file electronically with the Securities and Exchange Commission. You may access the registration statement of which this prospectus is a part at the Securities and Exchange Commission's Internet website. Upon closing of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934, as amended, and we will file reports, proxy statements and other information with the Securities and Exchange Commission.

This prospectus includes statistical data that were obtained from industry publications. These industry publications generally indicate that the authors of these publications have obtained information from sources believed to be reliable but do not guarantee the accuracy and completeness of their information. While we believe these industry publications to be reliable, we have not independently verified their data.

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
PTC Therapeutics, Inc.:

We have audited the accompanying balance sheets of PTC Therapeutics, Inc. (a development-stage company) as of December 31, 2004 and 2005, and the related statements of operations, stockholders' equity (deficit) and comprehensive loss, and cash flows for each of the years in the three-year period ended December 31, 2005 and for the period from March 31, 1998 (inception) to December 31, 2005. 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. The cumulative statements of operations, stockholders' equity (deficit) and comprehensive loss, and cash flows for the period from March 31, 1998 (inception) to December 31, 2005 include amounts for the period from March 31, 1998 (inception) to December 31, 1998 and for each of the years in the three-year period ended December 31, 2001, which were audited by other auditors who have ceased operations. Those auditors expressed an unqualified opinion on those financial statements, before the restatement described in note 2(o) to the financial statements, in their report dated March 22, 2002. Our opinion, insofar as it relates to the amounts included for the period from March 31, 1998 (inception) to December 31, 2001 before the restatement described in note 2(o), is based solely on the report of the other auditors.

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, based on our audits and the report of the other auditors, the financial statements referred to above present fairly, in all material respects, the financial position of PTC Therapeutics, Inc. (a development-stage company) as of December 31, 2004 and 2005, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2005 and for the period from March 31, 1998 (inception) to December 31, 2005, in conformity with U.S. generally accepted accounting principles.

As discussed above, the cumulative statements of operations, stockholders' equity (deficit) and comprehensive loss, and cash flows for the period from March 31, 1998 (inception) to December 31, 2005 include amounts for the period from March 31, 1998 (inception) to December 31, 2001, which were audited by other auditors who have ceased operations. As described in note 2(o), those financial statements have been restated. We audited the adjustments described in note 2(o) that were applied to restate the cumulative financial statements for the period from March 31, 1998 (inception) to December 31, 2001. In our opinion, such adjustments are appropriate and have been properly applied. However, we were not engaged to audit, review, or apply any procedures to the cumulative financials statements for the period from March 31, 1998 (inception) to December 31, 2001 of PTC Therapeutics, Inc. other than with respect to such adjustments, and, accordingly, we do not express an opinion or any other form of assurance on the cumulative financial statements for the period from March 31, 1998 (inception) to December 31, 2001 taken as a whole.

/s/ KPMG LLP

Philadelphia, Pennsylvania
March 31, 2006

The following is a copy of a report issued by Arthur Andersen LLP report for the fiscal year ended December 31, 2001 issued on March 22, 2002. This report has not been reissued by Arthur Andersen LLP, and Arthur Andersen LLP has not consented to its use in this Registration Statement on Form S-1.

Report of Independent Public Accountants

To the Stockholders and Board of Directors of
PTC Therapeutics, Inc.:

We have audited the accompanying balance sheets of PTC Therapeutics, Inc. (a Delaware corporation in the development stage) as of December 31, 2000 and 2001, and the related statements of operations, stockholders' equity (deficit), and cash flows for the years ended December 31, 2000 and 2001, and the period from inception (March 31, 1998) through December 31, 2001. 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 auditing standards generally accepted in the 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 financial position of PTC Therapeutics, Inc. as of December 31, 2000 and 2001, and the results of its operations and its cash flows for the years ended December 31, 2000 and 2001, and the period from inception (March 31, 1998) through December 31, 2001, in conformity with accounting principles generally accepted in the United States.

/s/ Arthur Andersen LLP

Philadelphia, Pennsylvania
March 22, 2002

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

BALANCE SHEETS
December 31, 2004 and 2005 and Pro Forma December 31, 2005

	2004	2005	Pro Forma 2005 (unaudited) (see note 2(u))
ASSETS			
Current assets:			
Cash and cash equivalents	$ 6,777,339	$ 10,964,552	$ 10,964,552
Short-term investments	26,209,351	26,875,682	26,875,682
Prepaid expenses and other current assets	721,941	1,136,755	1,136,755
Total current assets	33,708,631	38,976,989	38,976,989
Fixed assets, net	5,205,361	4,701,786	4,701,786
Deposits and other assets	54,049	295,704	295,704
Total assets	$ 38,968,041	43,974,479	43,974,479
LIABILITIES AND STOCKHOLDERS' EQUITY			
Current liabilities:			
Accounts payable	$ 1,703,026	$ 1,183,261	$ 1,183,261
Accrued expenses	1,500,875	2,710,366	2,710,366
Current portion of long-term debt	924,516	477,808	477,808
Deferred revenue	—	275,000	275,000
Total current liabilities	4,128,417	4,646,435	4,646,435
Deferred rent	21,441	122,653	122,653
Long-term debt	204,975	804,473	804,473
Total liabilities	4,354,833	5,573,561	5,573,561
Commitments and contingencies (note 9)			
Stockholders' equity:			
Preferred stock, $0.001 par value, authorized 153,407,582 shares;			
Series A convertible preferred stock, designated 750,000 shares issued and outstanding 750,000 shares actual (liquidation preference of $750,000); no shares issued and outstanding pro forma	750,000	750,000	—
Series B convertible preferred stock, designated 187,500 shares issued and outstanding 187,500 shares actual (liquidation preference of $375,000); no shares issued and outstanding pro forma	364,524	364,524	—
Series C convertible preferred stock, designated 6,295,000 shares issued and outstanding 6,000,000 shares actual (liquidation preference of $15,000,000); no shares issued and outstanding pro forma	14,117,089	14,117,089	—
Series D convertible preferred stock, designated 13,800,000 shares issued and outstanding 13,095,769 shares actual (liquidation preference of $42,561,249); no shares issued and outstanding pro forma	39,282,460	39,282,460	—
Series E convertible preferred stock, designated 128,242,850 shares issued and outstanding 125,740,607 shares actual (liquidation preference of $49,999,998); no shares issued and outstanding pro forma	49,048,047	49,048,047	—
Series E-2 convertible preferred stock, designated 4,132,232 shares issued and outstanding 3,670,138 shares actual (liquidation preference of $26,645,187); no shares issued and outstanding pro forma	—	26,510,745	—
Common stock, $0.001 par value; authorized 18,228,538 shares; issued and outstanding 68 shares at December 31, 2004 and 6,943 shares at December 31, 2005 and 13,511,665 issued and outstanding pro forma (unaudited)	—	7	13,512
Additional paid-in capital	353,131	506,364	130,565,724
Accumulated other comprehensive loss	(65,429)	(33,972)	(33,972)
Deficit accumulated during the development stage	(69,236,614)	(92,144,346)	(92,144,346)
Total stockholders' equity	34,613,208	38,400,918	38,400,918
Total liabilities and stockholders' equity	$ 38,968,041	$ 43,974,479	$ 43,974,479

See accompanying notes to financial statements.

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

STATEMENTS OF OPERATIONS
Years Ended December 31, 2003, 2004, and 2005, and for the Period from March 31, 1998 (inception) to December 31, 2005

	Year Ended December 31,			Period from March 31, 1998 (inception) to December 31,
	2003	2004	2005	2005
Revenues	$ 756,101	$ 1,606,076	$ 4,966,779	$ 7,668,956
Operating expenses:				
Research and development	17,694,414	20,070,231	21,122,934	76,970,532
General and administrative	4,693,240	6,022,740	7,943,584	27,230,732
Total operating expenses	22,387,654	26,092,971	29,066,518	104,201,264
Loss from operations	(21,631,553)	(24,486,895)	(24,099,739)	(96,532,308)
Interest income	316,827	578,732	853,817	3,997,886
Interest expense	(358,022)	(184,145)	(140,647)	(1,006,919)
Loss before tax benefit	(21,672,748)	(24,092,308)	(23,386,569)	(93,541,341)
Tax benefit	235,142	450,781	478,837	1,396,995
Net loss allocable to common stockholders	$ (21,437,606)	$ (23,641,527)	$ (22,907,732)	$ (92,144,346)
Basic and diluted net loss per share allocable to common stockholders	$ (315,259)	$ (347,670)	$ (9,925)	
Shares used to compute basic and diluted net loss per share allocable to common stockholders	68	68	2,308	
Pro forma basic and diluted net loss per common share (note 2(t)) (unaudited)			$ (2.11)	
Shares used to compute pro forma basic and diluted net loss per common share (note 2(t)) (unaudited)			10,831,634	

See accompanying notes to financial statements.

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT) AND COMPREHENSIVE LOSS
Period from March 31, 1998 (inception) to December 31, 2005

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Series C Convertible Preferred Stock		Series D Convertible Preferred Stock		Series E Convertible Preferred Stock	
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount
Initial capitalization, March 31, 1998	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —
Issuance of common stock	—	—	—	—	—	—	—	—	—	—
Sale of Series A convertible preferred stock	750,000	750,000	—	—	—	—	—	—	—	—
Deferred compensation	—	—	—	—	—	—	—	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	—
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1998	750,000	750,000	—	—	—	—	—	—	—	—
Deferred compensation	—	—	—	—	—	—	—	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	—
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 1999	750,000	750,000	—	—	—	—	—	—	—	—
Sales of Series B convertible preferred stock, net of issuance costs of $10,476	—	—	187,500	364,524	—	—	—	—	—	—
Sales of Series C convertible preferred stock, net of issuance costs of $882,911	—	—	—	—	6,000,000	14,117,089	—	—	—	—
Issuance of common stock	—	—	—	—	—	—	—	—	—	—
Deferred compensation	—	—	—	—	—	—	—	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	—
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	—	—
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	—
Total comprehensive loss										
Balance, December 31, 2000	750,000	750,000	187,500	364,524	6,000,000	14,117,089	—	—	—	—
Sales of Series D convertible preferred stock, net of issuance costs of $2,286,789	—	—	—	—	—	—	12,295,769	37,674,460	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	—
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	—	—
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	—
Total comprehensive loss										
Balance, December 31, 2001	750,000	750,000	187,500	364,524	6,000,000	14,117,089	12,295,769	37,674,460	—	—
Exercise of stock options	—	—	—	—	—	—	—	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	—
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 2002	750,000	750,000	187,500	364,524	6,000,000	14,117,089	12,295,769	37,674,460	—	—
Exercise of stock options	—	—	—	—	—	—	—	—	—	—
Issuance of options to consultants	—	—	—	—	—	—	—	—	—	—
Issuance of Series D convertible preferred stock in connection with the termination of collaboration agreement	—	—	—	—	—	—	800,000	1,608,000	—	—
Sales of Series E convertible preferred stock, net of issuance costs of $803,782	—	—	—	—	—	—	—	—	88,018,430	34,196,218
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—
Balance, December 31, 2003	750,000	750,000	187,500	364,524	6,000,000	14,117,089	13,095,769	39,282,460	88,018,430	34,196,218
Exercise of stock options	—	—	—	—	—	—	—	—	—	—
Warrants issued for in-process research and development	—	—	—	—	—	—	—	—	—	—
Sales of Series E convertible preferred stock, net of issuance costs of $148,169	—	—	—	—	—	—	—	—	37,722,177	14,851,829
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	—	—
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	—
Total comprehensive loss										
Balance, December 31, 2004	750,000	750,000	187,500	364,524	6,000,000	14,117,089	13,095,769	39,282,460	125,740,607	49,048,047
Exercise of stock options	—	—	—	—	—	—	—	—	—	—
Warrants issued for in-process research and development	—	—	—	—	—	—	—	—	—	—
Sales of Series E-2 convertible preferred stock, net of issuance costs of $134,441	—	—	—	—	—	—	—	—	—	—
Comprehensive loss:										
Net loss	—	—	—	—	—	—	—	—	—	—
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	—
Total comprehensive loss										
Balance, December 31, 2005	750,000	$ 750,000	187,500	$ 364,524	6,000,000	$ 14,117,089	13,095,769	$ 39,282,460	125,740,607	$ 49,048,047

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT) AND COMPREHENSIVE LOSS—(Continued)

	Series E-2 Convertible Preferred Stock		Common Stock						
	Shares	Amount	Shares	$0.001 Par Value	Additional Paid-in Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss)	Deficit Accumulated During the Development-Stage	Total Stockholders' Equity (Deficit)
Initial capitalization, March 31, 1998	—	$ —	59	$ —	$ 1,000	$ —	$ —	$ —	$ 1,000
Issuance of common stock	—	—	2	—	42	—	—	—	42
Sale of Series A convertible preferred stock	—	—	—	—	—	—	—	—	750,000
Deferred compensation	—	—	—	—	197	(197)	—	—	—
Amortization of deferred compensation	—	—	—	—	—	49	—	—	49
Net loss and comprehensive loss	—	—	—	—	—	—	—	(322,338)	(322,338)
Balance, December 31, 1998	—	—	61	—	1,239	(148)	—	(322,338)	428,753
Deferred compensation	—	—	—	—	197	(197)	—	—	—
Amortization of deferred compensation	—	—	—	—	—	86	—	—	86
Net loss and comprehensive loss	—	—	—	—	—	—	—	(671,055)	(671,055)
Balance, December 31, 1999	—	—	61	—	1,436	(259)	—	(993,393)	(242,216)
Sales of Series B convertible preferred stock, net of issuance costs of $10,476	—	—	—	—	—	—	—	—	364,524
Sales of Series C convertible preferred stock, net of issuance costs of $882,911	—	—	—	—	—	—	—	—	14,117,089
Issuance of common stock	—	—	1	—	7,812	—	—	—	7,812
Deferred compensation	—	—	—	—	98,381	(98,381)	—	—	—
Amortization of deferred compensation	—	—	—	—	—	64,279	—	—	64,279
Comprehensive loss:									
Net loss	—	—	—	—	—	—	—	(1,459,060)	(1,459,060)
Unrealized gain on investments	—	—	—	—	—	—	10,313	—	10,313
Total comprehensive loss									(1,448,747)
Balance, December 31, 2000	—	—	62	—	107,629	(34,361)	10,313	(2,452,453)	12,862,741
Sales of Series D convertible preferred stock, net of issuance costs of $2,286,789	—	—	—	—	—	—	—	—	37,674,460
Amortization of deferred compensation	—	—	—	—	—	26,466	—	—	26,466
Comprehensive loss:									
Net loss	—	—	—	—	—	—	—	(8,213,604)	(8,213,604)
Unrealized loss on investments	—	—	—	—	—	—	(10,313)	—	(10,313)
Total comprehensive loss									(8,223,917)
Balance, December 31, 2001	—	—	62	—	107,629	(7,895)	—	(10,666,057)	42,339,750
Exercise of stock options	—	—	6	—	40,000	—	—	—	40,000
Amortization of deferred compensation	—	—	—	—	—	7,895	—	—	7,895
Net loss and comprehensive loss	—	—	—	—	—	—	—	(13,491,424)	(13,491,424)
Balance, December 31, 2002	—	—	68	—	147,629	—	—	(24,157,481)	28,896,221
Exercise of stock options	—	—	—	—	775	—	—	—	775
Issuance of options to consultants	—	—	—	—	10,917	—	—	—	10,917
Issuance of Series D convertible preferred stock in connection with the termination of collaboration agreement	—	—	—	—	—	—	—	—	1,608,000
Sales of Series E convertible preferred stock, net of issuance costs of $803,782	—	—	—	—	—	—	—	—	34,196,218
Net loss and comprehensive loss	—	—	—	—	—	—	—	(21,437,606)	(21,437,606)
Balance, December 31, 2003	—	—	68	—	159,321	—	—	(45,595,087)	43,274,525
Exercise of stock options	—	—	—	—	643	—	—	—	643
Warrants issued for in-process research and development	—	—	—	—	193,167	—	—	—	193,167
Sales of Series E convertible preferred stock, net of issuance costs of $148,169	—	—	—	—	—	—	—	—	14,851,829
Comprehensive loss:									
Net loss	—	—	—	—	—	—	—	(23,641,527)	(23,641,527)
Unrealized loss on investments	—	—	—	—	—	—	(65,429)	—	(65,429)
Total comprehensive loss									(23,706,956)
Balance, December 31, 2004	—	—	68	—	353,131	—	(65,429)	(69,236,614)	34,613,208
Exercise of stock options	—	—	6,875	7	12,986	—	—	—	12,993
Warrants issued for in-process research and development	—	—	—	—	140,247	—	—	—	140,247
Sales of Series E-2 convertible preferred stock, net of issuance costs of $134,441	3,670,138	26,510,745	—	—	—	—	—	—	26,510,745
Comprehensive loss:									
Net loss	—	—	—	—	—	—	—	(22,907,732)	(22,907,732)
Unrealized gain on investments	—	—	—	—	—	—	31,457	—	31,457
Total comprehensive loss									(22,876,275)
Balance, December 31, 2005	3,670,138	$ 26,510,745	6,943	$ 7	$ 506,364	$ —	$ (33,972)	$ (92,144,346)	$ 38,400,918

See accompanying notes to financial statements.

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

STATEMENTS OF CASH FLOWS
Years Ended December 31, 2003, 2004, and 2005, and for the Period from March 31, 1998 (inception) to December 31, 2005

	Year Ended December 31,			Period from March 31, 1998 (inception) to December 31,
	2003	2004	2005	2005
Cash flows from operating activities:				
Net loss allocable to common stockholders	$ (21,437,606)	$ (23,641,527)	$ (22,907,732)	$ (92,144,346)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	1,553,029	1,437,444	1,466,131	6,325,046
In-process research and development charge	1,608,000	193,167	140,247	1,941,414
Stock-based compensation expense	10,917	—	—	109,692
Issuance of common stock for license	—	—	—	7,812
Realized gain on investment	—	—	—	(10,314)
Gain on disposal of fixed assets	(2,768)	—	—	(2,768)
Forgiveness of related-party loan	—	50,000	50,000	100,000
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	157,788	(443,388)	(414,814)	(1,086,755)
Deposits and other assets	19,970	(5,617)	(241,655)	(295,704)
Accounts payable	376,275	565,409	(397,790)	1,183,261
Accrued expenses	1,513,238	(454,012)	1,209,491	2,710,366
Deferred rent	(24,185)	(109,183)	101,212	122,653
Deferred revenue	—	—	275,000	275,000
Net cash used in operating activities	(16,225,342)	(22,407,707)	(20,719,910)	(80,764,643)
Cash flows from investing activities:				
Purchases of fixed assets	(667,491)	(1,120,810)	(962,556)	(11,039,173)
Purchases of investments	(11,038,405)	(51,671,306)	(34,741,738)	(177,586,492)
Sales of investments	25,374,112	32,623,927	34,106,864	150,687,151
Issuance of related-party loan	(50,000)	(50,000)	(50,000)	(150,000)
Net cash used in investing activities	13,618,216	(20,218,189)	(1,647,430)	(38,088,514)
Cash flows from financing activities:				
Proceeds from long-term debt	—	317,080	1,366,678	7,825,587
Payments on long-term debt	(1,974,286)	(1,866,128)	(1,213,888)	(6,528,196)
Proceeds from sale of Series A preferred stock	—	—	—	750,000
Proceeds from sale of Series B preferred stock, net of issuance costs	—	—	—	364,524
Proceeds from sale of Series C preferred stock, net of issuance costs	—	—	—	14,117,089
Proceeds from sale of Series D preferred stock, net of issuance costs	—	—	—	37,674,460
Proceeds from sale of Series E preferred stock, net of issuance costs	34,196,218	14,851,829	—	49,048,047
Proceeds from sale of Series E-2 preferred stock, net of issuance costs	—	—	26,510,745	26,510,745
Net proceeds from issuance of common stock	775	643	12,993	55,453
(Payments on) proceeds from short-term borrowings	—	121,975	(121,975)	—
Net cash provided by financing activities	32,222,707	13,425,399	26,554,553	129,817,709
Net increase (decrease) in cash and cash equivalents	29,615,581	(29,200,497)	4,187,213	10,964,552
Cash and cash equivalents, beginning of period	6,362,255	35,977,836	6,777,339	—
Cash and cash equivalents, end of period	$ 35,977,836	$ 6,777,339	$ 10,964,552	$ 10,964,552
Supplemental disclosure:				
Cash paid for interest	$ 358,022	$ 186,434	$ 138,770	$ 1,007,331
Unrealized gain (loss) on investments	—	(65,429)	31,457	(33,972)
Issuance of Series D preferred stock for in-process research and development	1,608,000	—	—	1,608,000
Issuance of warrants for in-process research and development	—	193,167	140,247	333,414
Acquisition of fixed assets through capital leases	—	—	—	15,110

See accompanying notes to financial statements.

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

NOTES TO FINANCIAL STATEMENTS
December 31, 2004 and 2005

(1) The Company

PTC Therapeutics, Inc. (the Company) was incorporated as a Delaware corporation on March 31, 1998. The Company is in the development-stage and is a biopharmaceutical company focused on the discovery and development of orally administered, proprietary small-molecule drugs that target post-transcriptional control processes.

The Company is devoting substantially all of its efforts toward product research and development, initial sales and market development, and raising capital. The Company has not generated product revenue to date and is subject to a number of risks similar to those of other development-stage companies, including dependence on key individuals, the development of commercially usable products, the need to obtain adequate additional financing necessary to fund the development of its products, and competition from larger companies. The Company has incurred losses each year since inception. As of December 31, 2005, the Company had a deficit accumulated during the development stage of $92.1 million. Given its planned level of operating expenses, management believes that its existing cash and cash equivalents and short-term investments, expected revenue from collaborations, grants, and interest income should be sufficient to meet its operating and capital requirements at least through 2007.

The Company may require amounts of additional capital in the future to fund operations, and the Company does not have any assurance that funding will be available when needed or on terms that the Company finds favorable, if at all. If the Company is unable to raise additional capital when required, the Company may need to delay, scale back, or eliminate some of its research and development programs.

(2) Summary of Significant Accounting Policies

(a) Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management 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.

(b) Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with a maturity of 90 days or less at the time of purchase to be cash equivalents. Cash equivalents are carried at market value.

(c) Investments

The Company’s short-term investments consist of debt securities. Management determines the classification of debt securities at the time of purchase and re-evaluates such designation as of each balance sheet date. Management cannot definitively state that it has the ability and intent to hold its short-term investments to maturity. As such, these investments are classified as available-for-sale and carried at fair market value, with any unrealized gain or loss recorded as a separate component of stockholders’ equity. As of December 31, 2004 and 2005, the Company has held all of its short-term investments to maturity. Fair value is based upon market prices quoted on the last day of the fiscal quarter.

The Company reviews its short-term investments on a periodic basis for other-than-temporary impairments. This review is subjective, as it requires management to evaluate whether an event or change in circumstances has occurred in that period that may have a significant adverse effect on the fair value of the

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

NOTES TO FINANCIAL STATEMENTS—(Continued)

investment. As of December 31, 2005, the Company has deemed its unrealized loss not to be other-than-temporary.

Following is a summary of investments accounted for as available-for-sale securities at December 31, 2004 and 2005:

	December 31, 2004			
		Unrealized		
	Cost	Gains	Losses	Estimated Fair Value
December 31, 2004:				
Commercial paper	$ 996,657	$ —	$ (617)	$ 996,040
U.S. corporate debt securities	23,089,766	—	(64,745)	23,025,021
U.S. government debt securities	2,188,357	35	(102)	2,188,290
Total short-term investments	$ 26,274,780	$ 35	$ (65,464)	$ 26,209,351

	December 31, 2005			
		Unrealized		
	Cost	Gains	Losses	Estimated Fair Value
December 31, 2005:				
Commercial paper	$ 1,497,124	$ —	$ —	$ 1,497,124
U.S. corporate debt securities	25,412,530	—	(33,972)	25,378,558
Total short-term investments	$ 26,909,654	$ —	$ (33,972)	$ 26,875,682

All investments on the balance sheet at December 31, 2005 mature in 2006.

(d) Depreciation and Amortization

Depreciation and amortization are computed using the straight-line method based on the shorter of the estimated useful life of the related asset, or the lease term after considering renewals, as follows:

Lab leasehold improvements	7 years
Computer equipment and software	3 years
Furniture, fixtures and lab equipment	3 to 7 years
Leasehold improvements	7 years

Depreciation and amortization expense was $1,553,029, $1,437,444, $1,466,131, and $6,325,046 for the years ended December 31, 2003, 2004, and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, respectively.

(e) Concentration of Credit Risk

The Company has no significant off-balance-sheet risk or credit risk concentrations. The Company maintains its cash, cash equivalents and short-term investments with various established financial institutions. The Company invests its excess funds primarily in government bonds and “A” rated, or better, corporate bonds.

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

NOTES TO FINANCIAL STATEMENTS—(Continued)

(f) Deferred Rent

The Company has several operating leases for office space and office equipment. Under the terms of the office building lease, the Company was entitled to $166,000 of lease incentives as a reimbursement for leasehold improvements. In addition, four months of lease incentives totaling $125,000 were included in the initial lease terms. Two months of lease incentives were taken at the beginning of the lease in 2004 and two will be taken at the end of the lease in 2009, The remaining rent due on the lease, after incentives, is spread evenly over the lease period and recorded as rent expense. The difference between the actual cash paid and the rent expense is recorded as deferred rent.

(g) Revenue Recognition

Revenues represent grant proceeds and income from a collaboration agreement. The Company records deferred revenue for amounts received upfront under collaboration agreements in which they have continuing involvement, and the Company recognizes such deferred amounts as revenue ratably over the estimated contract performance period. Such revenue recognition may be accelerated in the event of contract termination prior to completion of the expected performance period. Milestone fees are recorded as revenue when the milestone event is achieved. Grant revenues are recognized as the cash is received or when the related preclinical, clinical or regulatory milestones are met.

(h) Research and Development Costs

Research and development expenses include the clinical development costs associated with the Company's product development programs and research and development costs associated with the Company's discovery programs. These expenses include internal research and developments costs and the costs of research and development conducted on behalf of the Company by third parties, including sponsored university-based research agreements and clinical study vendors. All research and development costs are expensed as incurred. Costs incurred in obtaining technology licenses are charged immediately to research and development expense if the technology licensed has not reached technological feasibility and has no alternative future uses. For the years ended December 31, 2003, 2004, and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, the Company recorded in-process research and development charges of $1,608,000, $193,167, $140,247, and $1,941,414, respectively, related to a license agreement (see note 9).

(i) Fair Value of Financial Instruments

Cash and cash equivalents, short-term investments and accounts payable are reflected in the accompanying financial statements at fair value due to the short-term nature of those instruments. The carrying amounts of the Company's debt obligations approximate their fair values as of each of the balance sheet dates based upon the interest rates on recent borrowings.

(j) Impairment of Long-Lived Assets

The Company assesses the recoverability of long-lived assets by determining whether the carrying value of such assets can be recovered through the sum of the undiscounted future operating cash flows and cash flows from the eventual disposition of the asset. If impairment is indicated, the Company measures the amount of such impairment by comparing the carrying value of the assets to the fair value of these assets, generally determined based on the present value of the expected future cash flows associated with the assets. Although current and historical negative cash flows are indicators of impairment, management believes the future cash flows to be received from the long-lived assets and the ultimate success of the Company's research

PTC THERAPEUTICS, INC.
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NOTES TO FINANCIAL STATEMENTS—(Continued)

programs will exceed the assets' carrying value, and accordingly, the Company has not recognized any impairment losses through December 31, 2005.

(k) Stock-Based Compensation

The Company has elected to account for its employee stock-based compensation plans following Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations rather than the alternative fair value accounting provided under Statement of Financial Accounting Standards (SFAS) No. 123, *Accounting for Stock-Based Compensation* (see note 8).

The Company has adopted the disclosure provisions of SFAS No. 123, as amended by SFAS No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure*. The following table illustrates the effect on the net loss if the fair-value-based method had been applied to all outstanding and unvested awards in each period.

	Year Ended December 31,			Period from March 31, 1998 (inception) to December 31,
	2003	2004	2005	2005
Net loss allocable to common stockholders, as reported	$ (21,437,606)	$ (23,641,527)	$ (22,907,732)	$ (92,144,346)
Deduct total stock-based employee compensation expense determined under fair-value-based method for all awards	(33,656)	(25,603)	(464,570)	(594,563)
Pro forma net loss allocable to common stockholders	$ (21,471,262)	$ (23,667,130)	$ (23,372,302)	$ (92,738,909)
Basic and diluted net loss per share allocable to common stockholders, as reported	$ (315,259)	$ (347,670)	$ (9,925)	
Pro forma basic and diluted loss per share allocable to common stockholders	$ (315,754)	$ (348,046)	$ (10,127)	

The Company has computed the pro forma disclosures required under SFAS No. 123 using the Black-Scholes option-pricing model prescribed by SFAS No. 123. There were 2,106,803 options granted in 2005. The weighted average fair value of options granted during 2003 and 2005 is $0.04 per share and $0.31 per share, respectively. There were no stock option grants in 2004. The fair value of each option grant in 2003 and 2005 was estimated on the date of grant with the following assumptions:

	2003	2005
Risk-free interest rate	2.53%	3.62%
Expected life	5	5
Dividend yield	0%	0%
Expected volatility	0%	0%

PTC THERAPEUTICS, INC.
(A Development-Stage Company)

NOTES TO FINANCIAL STATEMENTS—(Continued)

(l) Income Taxes

The Company accounts for income taxes under the asset and liability method in accordance with SFAS No. 109, *Accounting for Income Taxes*. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the statement of operations in the period that includes the enactment date.

(m) Recently Issued Accounting Standards

In December 2004, the Financial Accounting Standards Board (FASB) issued SFAS No. 123(R), *Share-Based Payment*. SFAS No. 123(R) supersedes SFAS No. 123, APB Opinion No. 25 and its related implementation guidance. SFAS No. 123(R) will require compensation costs related to share-based payment transactions to be recognized in the financial statements. The amount of compensation cost will be measured based on the grant-date fair value of the equity or liability instruments issued. Compensation cost will be recognized over the period that an employee provides service in exchange for the award. SFAS No. 123(R) is effective as of the beginning of the first interim or annual reporting period that begins after December 15, 2005. The Company has not yet determined the impact that implementing SFAS No. 123(R) will have on the Company's results of operations or financial condition.

In June 2005, the FASB issued SFAS No. 154, *Accounting Changes and Error Corrections*. This statement requires that a voluntary change in accounting principle be applied retrospectively with all prior period financial statements presented on the basis of the new accounting principle, unless it is impracticable to do so. SFAS No. 154 also provides that (1) a change in method of depreciating or amortizing a long-lived nonfinancial asset be accounted for as a change in estimate (prospectively) that was effected by a change in accounting principle, and (2) correction of errors in previously issued financial statements should be termed a "restatement." The new standard is effective for accounting changes and correction of errors made in fiscal years beginning after December 15, 2005. Early adoption of this standard is permitted for accounting changes and correction of errors made in fiscal years beginning after June 1, 2005. The Company does not anticipate that the adoption of this statement will have a material impact on the Company's results of operation or financial condition.

In November 2005, the FASB issued FASB Staff Position FAS 115-1 and FAS 124-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments* (FSP). The FSP addresses the determination as to when an investment is considered impaired, whether that impairment is other than temporary and the measurement of an impairment loss. The FSP also includes accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. The guidance in the FSP is required to be applied to reporting periods beginning after December 15, 2005. The Company will adopt the provisions of this FSP in 2006 and does not currently believe that implementation will have a material effect on the results of the Company's operations or financial condition.

(n) Segment Information

The Company is managed and operated as one business. The Company is managed by a single management team that reports to the chief executive officer. The Company does not operate separate lines of business or separate business entities with respect to any of its product candidates. Accordingly, the Company does not prepare discrete financial information with respect to separate product areas, or by location, and does not have separately reportable segments.

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(o) Restatement

During the year ended December 31, 2002, the Company restated its 2001 financial statements to properly account for its investments. The Company previously reported its investments at cost instead of amortized cost. The restatement resulted in a decrease to interest income and an increase in net loss and deficit accumulated during the development stage of $275,452.

(p) Reclassifications

Certain reclassifications have been made to the 2003 and 2004 financial statements and the financials statements for the period from March 31, 1998 (inception) to December 31, 2005 to conform to the 2005 presentation.

(q) Advertising Costs

Advertising costs are charged to expense as incurred.

(r) Patent Costs

Patent costs are charged to expense as incurred.

(s) Net Loss per Share

Net loss per share is computed in accordance with SFAS No. 128, *Earnings per Share*, by dividing the net loss allocable to common stockholders by the weighted average number of shares of common stock outstanding.

As of December 31, 2005, the Company has outstanding certain options, warrants and convertible preferred stock (see notes 7 and 8), which have not been used in the calculation of diluted net loss per share because to do so would be anti-dilutive. Anti-dilutive instruments totaled approximately 7,991,000, 10,112,000, and 15,847,000 at December 31, 2003, 2004, and 2005, respectively. As such, the numerator and the denominator used in computing both basic and diluted net loss per share allocable to common stockholders are equal.

(t) Pro Forma Net Loss per Share (Unaudited)

The following pro forma basic and diluted net loss per share allocable to common stockholders and shares used in computing pro forma basic and diluted net loss per share allocable to common stockholders have been presented reflecting the assumed automatic conversion into shares of common stock of the convertible

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preferred stock upon completion of the planned initial public offering (the Offering) (see note 7), using the if converted method from their respective dates of issuance:

	Year Ended December 31, 2005 (unaudited)
Net loss allocable to common stockholders	$ (22,907,732)
Weighted average shares used in computing basic and diluted net loss per share	2,308
Basic and diluted net loss per common share	$ (9,925)
Pro forma (unaudited):	
Shares used above	2,308
Pro forma adjustment to reflect weighted effect of assumed conversion of convertible preferred stock	10,829,326
Shares used in computing pro forma basic and diluted net loss per common share	10,831,634
Pro forma basic and diluted net loss per common share (unaudited)	$ (2.11)

(u) Pro Forma Balance Sheet (Unaudited)

Upon the closing of the Offering, all of the outstanding shares of convertible preferred stock as of December 31, 2005 will automatically convert into 13,504,722 shares of common stock (see note 7). The December 31, 2005 unaudited pro forma balance sheet has been prepared assuming the automatic conversion of the convertible preferred stock outstanding as of December 31, 2005 into common stock.

(3) Income Taxes

The effective tax rate varies from the U.S. federal statutory tax rate for the years ended December 31, 2003, 2004, and 2005 principally due to the following:

	2003		2004		2005	
	Amount	%	Amount	%	Amount	%
U.S. Federal statutory tax	$ (7,288,786)	(34.0)%	$ (8,191,385)	(34.0)%	$ (7,951,433)	(34.0)%
Add (deduct):						
Sale of state net operating losses	(235,142)	(1.1)	(450,781)	(1.9)	(478,837)	(2.0)
State tax benefit on deferred taxes	—	—	(2,817,428)	(11.7)	(2,895,164)	(12.4)
Federal research and development credits	(782,985)	(3.7)	(910,000)	(3.8)	(1,119,567)	(4.8)
Change in valuation allowance	8,060,518	37.6	11,903,786	49.4	11,927,854	51.0
Other net	11,253	0.1	15,027	0.1	38,310	0.2
Tax benefit	$ (235,142)	(1.1)%	$ (450,781)	(1.9)%	$ (478,837)	(2.0)%

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NOTES TO FINANCIAL STATEMENTS—(Continued)

The components of the Company's deferred tax assets and liabilities at December 31, 2004 and 2005 are as follows:

	2004	2005
Deferred tax assets		
Amortization	$ 197,739	$ 185,447
Accruals	86,416	186,250
Federal tax credits	2,592,037	3,711,604
State tax credits	1,959,903	2,825,245
Federal net operating losses	15,399,753	18,178,386
State net operating losses	3,874,728	4,554,412
Capitalized research and development costs	9,541,084	15,625,393
Other	125,317	217,901
	33,776,977	45,484,638
Valuation allowance	(33,522,215)	(45,450,069)
Total assets	254,762	34,569
Deferred tax liabilities:		
Depreciation	(254,762)	(34,569)
Total liabilities	(254,762)	(34,569)
Net deferred tax asset	$ —	$ —

The increase in the valuation allowance during the years ended December 31, 2003, 2004, and 2005 was approximately $8,061,000, $11,904,000, and $11,928,000, respectively. At December 31, 2004 and 2005, the Company had recorded a full valuation allowance against its net deferred tax asset of approximately $33,522,000 and $45,450,000, respectively, as management believes it cannot at this time conclude that it is more likely than not they will be realized.

As of December 31, 2004 and 2005, the Company has approximately $44,763,000 and $52,536,000, respectively, of federal net operating loss carryforwards, and $41,914,000 and $49,687,000, respectively, of state net operating loss carryforwards. As of December 31, 2005, credit carryforwards for federal and state purposes are $3,712,000 and $2,825,000, respectively. The federal net operating loss carryforwards expire beginning in 2018, while the federal credit carryforwards expire beginning in 2013. Both are subject to review and possible adjustment by the Internal Revenue Service. State net operating loss carryforwards begin to expire in 2009 and the state credit carryforwards begin to expire in 2015. The *Internal Revenue Code* contains provisions that may limit the net operating loss and credit carryforwards available to be used in any given year given certain historical changes in the ownership interests of significant stockholders.

During the years ended December 31, 2003, 2004, and 2005, the Company sold $271,841, $521,134, and $547,242, respectively, of New Jersey state net operating loss carryforwards to a third-party. Accordingly, the Company recorded income tax benefits and received cash for the years ended December 31, 2003, 2004 and 2005 in the amount of $235,142, $450,781, and $478,837, respectively.

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NOTES TO FINANCIAL STATEMENTS—(Continued)

(4) Fixed Assets, Net

Fixed assets, net were as follows at December 31, 2004 and 2005:

	2004	2005
Lab leasehold improvements	$ 1,763,281	$ 1,763,281
Computer equipment and software	1,629,726	1,766,827
Furniture and fixtures and lab equipment	5,603,508	6,190,666
Leasehold improvements	802,785	1,011,723
Construction in progress	249,733	279,092
	10,049,033	11,011,589
Less accumulated depreciation	(4,843,672)	(6,309,803)
	$ 5,205,361	$ 4,701,786

(5) Accrued Expenses

Accrued expenses at December 31, 2004 and 2005 consist of the following:

	2004	2005
Employee compensation, benefits, and related accruals	$ 832,070	$ 1,113,030
Consulting and contracted research	390,299	710,028
Professional fees	175,727	607,387
Other	102,779	279,921
	$ 1,500,875	$ 2,710,366

(6) Long-Term Debt

In March 2001, the Company entered into a $1,300,000 equipment facility agreement with a bank. The equipment facility bore interest at a fixed rate of 7.65%. Borrowings under this line were collateralized by certain of the Company's business assets. Under this agreement, the Company recorded interest expense of $30,482, $2,515, and $150,882 for the years ended December 31, 2003 and 2004 and the period from March 31, 1998 (inception) to December 31, 2005, respectively. This equipment facility matured on April 1, 2004.

In January 2002, the Company entered into an equipment line of credit with a lending institution. In accordance with the line of credit, the Company entered into a series of promissory notes in the aggregate amount of $4,824,414, which were collateralized by certain of the Company's fixed assets. These promissory notes carried fixed interest rates ranging from 9.51% to 9.83%. The Company recorded interest expense of $327,201, $171,885, $29,427, and $721,316 for the years ended December 31, 2003, 2004, and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, respectively, related to these promissory notes. In connection with the promissory notes, in 2002 the Company issued warrants to purchase 59,378 shares of the Company's common stock (see note 7). At the time of issuance, the fair value of the warrants was determined to be immaterial. The notes matured in 2005.

In June 2004, the Company entered into an equipment line of credit with a lending institution. In accordance with the line of credit, the Company entered into two promissory notes in 2004 for an aggregate amount of $317,080 and four promissory notes in the aggregate amount of $1,366,678 in 2005, all of which are collateralized by certain of the Company's fixed assets. These promissory notes carry fixed interest rates

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NOTES TO FINANCIAL STATEMENTS—(Continued)

ranging from 9.55% to 10.30% and are payable in fixed monthly installments. The Company recorded interest expense of $9,745, $111,220, and $120,965 for the years ended December 31, 2004 and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, respectively, related to these promissory notes.

Short-term borrowings in 2004 included outstanding checks that were reclassified to accounts payable on the balance sheet at December 31, 2004.

Long-term debt maturities as of December 31, 2005 are as follows:

2006	$ 477,808
2007	512,712
2008	261,122
2009	30,639
	$ 1,282,281

(7) Stockholders' Equity

(a) Reverse Stock Split

In conjunction with the Series E financing, the Company effected a 30,000-for-1 reverse stock split of the common stock in 2004. As a result, the Company's issued and outstanding stock was reduced from 2,137,564 to 68 shares. The par value of the common stock was not affected by the reverse stock split and remains at $0.001 per share. Consequently, the aggregate par value of the issued common stock was reduced by reclassifying the par value amount of the eliminated shares of common stock to additional paid-in capital. Outstanding shares have been retroactively restated in the financial statements and in the notes to financial statements for all periods presented to reflect the reverse stock split.

(b) Founders' Common Stock

During 1998, the Company issued 59 shares of common stock to the two founders of the Company for consideration representing the fair market value of the shares. The Company also issued two shares of common stock to a university in exchange for an exclusive license. The license agreement had antidilution provisions. Under this provision, the Company issued an additional one share to the university during 2000 (see note 9).

The holders of the common stock are entitled to elect two members of the Board of Directors.

(c) Convertible Preferred Stock

As of December 31, 2005, the Company has authorized for issuance up to 153,407,582 shares of preferred stock, $0.001 par value. The authorized shares have been designated as follows: 750,000 shares of Series A convertible preferred stock (Series A), 187,500 shares of Series B convertible preferred stock (Series B), 6,295,000 shares of Series C convertible preferred stock (Series C), 13,800,000 shares of Series D convertible preferred stock (Series D), 128,242,850 shares of Series E convertible preferred stock (Series E), and 4,132,232 of Series E-2 convertible preferred stock (Series E-2).

The rights and preferences of the Series A, Series B, Series C, Series D, Series E, and Series E-2 are as follows:

Conversion— On a post-reverse-split basis, each share of Series A, Series B, Series C, Series D, Series E, and Series E-2 stock is convertible at the option of the holder into such number of shares of common stock as is determined by applying a factor to the outstanding shares of approximately 0.0833, 0.1333, 0.1389, 0.1548,

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0.0548, and 1.00 for the Series A, Series B, Series C, Series D, Series E, and Series E-2, respectively. These conversion factors are subject to adjustment in the event the Company engages in specified dilutive issuances of equity securities at prices below the applicable conversion factor, or if the Company engages in specified changes to its capitalization, such as stock splits or stock dividends. Prior to the issuance of Series E, each share of preferred stock was convertible into one share of common stock. The conversion becomes automatic upon the closing of an initial public offering in which not less than $50,000,000 of net proceeds shall be received by the Company, at a price per share for common stock that is at least equal to two times the Series E-2 price of $7.26 per share.

Voting— Each preferred shareholder is entitled to the number of votes per share as if the preferred shares were converted to common stock. Additionally, the holders of the preferred stock, voting as a single class, are entitled to elect four members of the Board of Directors.

Liquidation— Upon the liquidation, dissolution or winding-up of the Company, holders of preferred stock will be entitled to receive, before any distribution or payment is made on the common stock, an amount equal to $1.00 per share for Series A, $2.00 per share for Series B, $2.50 per share for Series C, $3.25 per share for Series D, $0.397644 per share for Series E, and $7.26 per share for Series E-2, plus all declared, but unpaid, dividends. As of December 31, 2005, the aggregate liquidation preference is $750,000, $375,000, $15,000,000, $42,561,249, $49,999,998, and $26,645,187 for the Series A, Series B, Series C, Series D, Series E, and Series E-2 stock, respectively. The Company has never declared any dividends.

(d) Warrants

In 2000, the Company issued warrants to purchase 295,000 shares of Series C stock for services rendered in connection with the Series C financing. The warrants vested immediately and have an exercise price of $2.50 per share. The warrants expire in 2010. At the date of grant, the fair value of the warrants was approximately $38,000.

In 2001, the Company issued a warrant to purchase one share of the Company's common stock for services rendered by a consultant. The warrant vested immediately and had an exercise price of $75,000. The fair market value of the warrant was immaterial. The warrant expired in 2005.

In 2001, the Company issued warrants to purchase 614,788 shares of Series D stock for services rendered in connection with the Series D financing. The warrants vested immediately and have an exercise price of $3.25 per share. The warrants expire in 2011. At the date of grant, the fair value of the warrants was approximately $37,000.

In 2002, the Company issued warrants (with antidilution protection) to purchase shares of the Company's common stock in connection with a debt financing (see note 6). The warrants vested immediately, and expire in 2009. In connection with the Series E financing in 2004, the Company and warrant holder agreed to cancel the existing common stock warrants and to replace them with Series D stock warrants to purchase 59,378 shares of Series D stock at $3.25 per share. At the date of grant, the fair value of the warrants was $5,000.

In 2003, the Company issued warrants (with antidilution protection) to purchase shares of common stock in connection with the termination of a collaboration agreement and acquisition of the related intangibles (see note 9). Based on adjustments to the conversion price resulting from the Series E financing and accounting for the subsequent reverse stock split, the warrants are exercisable for 77,380 shares of common stock as of December 31, 2005. The warrants vest upon the achievement of certain clinical milestones, the first of which was met in 2004 and a second milestone was met in 2005. As a result, on a split adjusted basis, warrants to purchase 38,690 and 23,214 shares of common stock vested, with related charges of $193,167, $140,247, and

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NOTES TO FINANCIAL STATEMENTS—(Continued)

$333,414 for the years ended December 31, 2004 and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, respectively.

In 2004, the Company issued warrants to purchase 994,415 shares of Series E preferred stock for services rendered in connection with the Series E financing. The warrants immediately vested with an exercise price of $0.3976 per share. At the date of grant, the fair value of the warrants was $395,000.

Unless otherwise noted, all warrants are outstanding as of December 31, 2005.

(8) Stock Option Plan

During 1998, the Company established the 1998 Stock Option Plan (the 1998 Plan), which provides for the granting of incentive stock options and nonqualified stock options. In 2005, the Board of Directors approved an additional 400,000 shares for grant under this plan. As of December 31, 2005, 254,168 options were available for grant. The Board of Directors has the authority to select the employees and nonemployees to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) the date on which the option becomes exercisable; (iii) the option exercise price, which, in the case of incentive stock options, must be at least 100% (110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's stock) of the fair market value of the common stock as of the date of grant; and (iv) the duration of the option (which, in the case of incentive stock options, may not exceed ten years). Options typically vest over a three- or four-year period. The options granted under the 1998 Plan expire no later than ten years from the date of grant.

A summary of stock option activity to employees and nonemployees is as follows:

	Number of Shares	Exercise Price	Weighted Average Exercise Price
Outstanding at March 31, 1998 (inception)	—	$ —	$ —
Granted	88	3,000-9,900	8,225.00
Exercised	(7)	6,000-7,500	6,005.00
Forfeited	(12)	6,000-9,900	6,809.00
Outstanding at December 31, 2002	69	3,000-9,900	8,692.00
Granted	25	9,900	9,900.00
Exercised	—	—	—
Forfeited	(1)	9,900	9,900.00
Outstanding at December 31, 2003	93	3,000-9,900	9,010.25
Granted	—	—	—
Exercised	—	—	—
Forfeited	—	—	—
Outstanding at December 31, 2004	93	3,000-9,900	9,010.25
Granted	2,106,803	1.89	1.89
Exercised	(6,875)	1.89	1.89
Forfeited	(35,063)	1.89-9,900	3.04
Outstanding at December 31, 2005	2,064,958	1.89-9,900	2.28
Exercisable at December 31, 2005	1,379,159	$ 1.89-9,900	$ 2.42

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NOTES TO FINANCIAL STATEMENTS—(Continued)

Exercise Price Range	Number of Options Outstanding	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Number of Options Exercisable	Weighted Average Exercise Price
$3,000-9,900	89	$ 8,145.65	6.21	81	$ 8,910.14
1.89	2,064,869	1.89	8.91	1,379,078	1.89
	2,064,958			1,379,159	

The Company issued common stock options in connection with the Company's stock plans to nonemployees. The Company recognized compensation expense related to these options of $10,917, $0, $0, and $109,692 for the years ended December 31, 2003, 2004, and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, respectively. Included in the above tables are fractional shares outstanding as a result of the 30,000-for-1 reverse stock split.

(9) Commitments and Contingencies

(a) Amgen SF, LLC (formerly Tularik, Inc.) Collaboration Agreement

In 1998, the Company entered into a collaboration agreement with Amgen SF, LLC (Amgen) to develop and market novel therapeutic products based on compounds identified from an established cooperative research relationship between the two parties. This research was being directed by the research management committee, which consists of representatives from both parties. Under this agreement, Amgen agreed to pay milestone payments upon the occurrence of certain events, as defined in the agreement.

In 2003, the Company received shareholder consent to terminate the existing collaboration agreement with Amgen and enter into a new license agreement. Under the terms of the license agreement, the Company received rights in the nonsense suppression field to specific compounds and intellectual property generated under the prior collaboration agreement. In exchange for these rights, the Company issued Amgen 800,000 shares of Series D stock and warrants for shares of common stock (see note 7). The preferred shares were 100% vested upon issuance and the warrants vest based on certain clinical milestones. The warrants will be valued using the Black-Scholes option-pricing model and the Company will record a noncash expense upon achievement of the milestones. The value of the Series D stock issued in connection with the agreement was determined by the Company's management. In 2004, the Company recorded a noncash in-process research and development charge of $193,167, in conjunction with the vesting of a portion of the warrants based upon the achievement of the first clinical milestone. The amount was immediately expensed due to the preclinical status of the related compounds and intellectual property rights acquired. In 2005, the Company recorded a noncash in-process research and development charge of $140,247 upon the achievement of the second clinical milestone. Based on adjustments to the conversion price resulting from the Series E financing and accounting for the subsequent reverse stock split, the net number of vested shares underlying these milestones was 38,690 and 61,904 at December 31, 2004 and 2005, respectively.

(b) University of Medicine and Dentistry of New Jersey Research, Option and License Agreement

In 1998, the Company entered into a Research, Option and License Agreement (the Agreement) with the University of Medicine and Dentistry of New Jersey (the University) that gives the Company the exclusive right to develop and commercialize products covered by certain licensed technology. As partial consideration for the licenses, the Company issued 4% (two shares with par value of $0.001) of its common stock to the University in 1998. The fair market value of the shares issued was charged to expense due to the uncertainty of the future uses of the technology. In 2000, the Company issued an additional share to the University to ensure that its ownership interest in the Company continued to comprise 4% of the outstanding

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capital stock on a fully diluted basis until a total of $2,000,000 was raised by the Company, as required by the Agreement. The Agreement requires the Company to remit royalty payments on the sale of products, if any covered by the licensed technology. If products are sold by third parties through sublicensing agreements, then the Company is obligated to remit a portion of the sublicensing income related to the licensed technology to the University.

(c) Consulting Agreements

The Company has signed various consulting agreements with individuals for services to be provided through 2006.

(d) Operating Leases

The Company leases office space under a noncancelable operating lease through July 2009. Rent expense was $246,942, $180,715, $319,088 and $1,169,582 for the years ended December 31, 2003, 2004 and 2005, and the period from March 31, 1998 (inception) to December 31, 2005, respectively. The Company also leases certain office equipment under operating leases. Future minimum lease payments as of December 31, 2005 are as follows:

2006	$	383,688
2007		393,763
2008		391,302
2009		169,688
	$	1,338,441

(e) Related-Party Transactions

The Company issued a loan in the amount of $50,000 in 2003 in connection with the hiring of an executive. This executive was entitled to two additional loans of $50,000 each to be issued upon the one- and two-year anniversary date of the first issuance. The Company agreed to forgive payment of the loans upon the one-year anniversary date of each of the loan issuances assuming the executive is still an employee of the Company. Principal and interest were forgiven under this loan upon the one-year anniversary date of issuance. A second loan in the amount of $50,000 was made in 2004 and, along with interest, forgiven upon the executive's two-year anniversary in 2005. A final loan in the amount of $50,000 was made in August 2005. This loan was forgiven on March 29, 2006. As of December 31, 2005, the loan is included in prepaid expenses and other current assets on the accompanying balance sheet.

(f) 401(k) Plans

The Company maintains 401(k) plans for its employees. Employee contributions are voluntary. The Company may match employee contributions in amounts to be determined at the Company's sole discretion. No contributions have been made by the Company from March 31, 1998 (inception) to December 31, 2005.


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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. *Other Expenses of Issuance and Distribution*

The following table indicates the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by the Registrant. All amounts are estimated except the Securities and Exchange Commission registration fee and the National Association of Securities Dealers Inc. filing fee.

	Amount
Securities and Exchange Commission registration fee	$ 9,229
National Association of Securities Dealers Inc. fee	9,125
Nasdaq Stock Market listing fee	*
Accountants' fees and expenses	*
Legal fees and expenses	*
Blue Sky fees and expenses	*
Transfer Agent's fees and expenses	*
Printing and engraving expenses	*
Miscellaneous	*
Total expenses	$ *

* To be filed by amendment.

Item 14. *Indemnification of Directors and Officers*

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. The Registrant's certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

The Registrant's restated certificate of incorporation provides that the Registrant will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action,

suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Registrant) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Registrant, or is or was serving, or has agreed to serve, at the Registrant's request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, including any employee benefit plan, (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity or in any other capacity while serving as a director, officer, partner, employee or trustee against all expenses (including attorneys' fees), liabilities, loss, judgments, fines, ERISA taxes or penalties and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the Registrant's best interests, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The Registrant's restated certificate of incorporation provides that the Registrant will indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Registrant to procure a judgment in the Registrant's favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer of the Registrant, or is or was serving, or has agreed to serve, at the Registrant's request, as a director, officer, partner, employee or trustee of or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity or in any other capacity while serving as a director, officer, partner, employee or trustee, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Registrant, except that no indemnification shall be made with respect to any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Registrant, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expense (including attorney's fees) which the Court of Chancery of Delaware or such other court shall deem proper. Notwithstanding the foregoing, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding, Indemnitee shall be indemnified by the Registrant against all expenses (including attorneys' fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

The Registrant maintains a general liability insurance policy that covers certain liabilities of the Registrant's directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

In any Underwriting Agreement that the Registrant enters into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, the Registrant, its directors, its officers and persons who control the Registrant within the meaning of the Securities Act of 1933, as amended, against certain liabilities.

Item 15. ***Recent Sales of Unregistered Securities***

Set forth below is information regarding shares of common stock and preferred stock issued, and options and warrants granted, by the Registrant within the past three years that were not registered under the Securities Act of 1933, as amended. Also included is the consideration, if any, received by the Registrant for such shares, options and warrants and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuances of Securities

1. In December 2003 and in April and June 2004, the Registrant issued an aggregate of 125,740,607 shares of Series E convertible preferred stock at a price of $.397644 per share, together with warrants to purchase an aggregate of 994,415 shares of Series E convertible preferred stock with an exercise price of $.397644 per share to institutional investors, including Credit Suisse Entities, HBM BioVentures (Cayman) Ltd., Vulcan Capital Venture Holdings Inc., Delphi Ventures Entities, Bay City Capital Entities, Novo A/ S and Three Crowns Capital (Bermuda) Ltd., for aggregate cash proceeds of approximately $50.0 million.

2. In September and October 2005, the Registrant issued an aggregate of 3,670,138 shares of Series E-2 convertible preferred stock at a price of $7.26 per share to institutional investors, including Credit Suisse Entities, HBM BioVentures (Cayman) Ltd., Vulcan Capital Venture Holdings Inc., Delphi Ventures Entities, Bay City Capital Entities and Novo A/ S, for aggregate cash proceeds of approximately $26.6 million.

3. In the first quarter of 2004, we issued to General Electric Capital Corporation a warrant to purchase 59,378 shares of our series D convertible preferred stock in exchange for the cancellation of a previously issued warrant to purchase shares of our common stock.

No underwriters were involved in the foregoing sales of securities. The securities described in this section (a) of Item 15 were issued to a combination of foreign and U.S. investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act and Rule 506 of Regulation D promulgated thereunder relative to sales by an issuer not involving any public offering, to the extent an exemption from such registration was required. All purchasers of shares of convertible preferred stock described above represented to the Registrant in connection with their purchase that they were accredited investors and were acquiring the shares for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

(b) Stock Option Grants

Since inception, the Registrant has issued options to certain employees, consultants and others to purchase an aggregate of 2,389,011 shares of common stock as of March 15, 2006. As of March 15, 2006, options to purchase 11,828 shares of common stock had been exercised, options to purchase 36,468 shares of common stock had been forfeited and options to purchase 2,340,715 shares of common stock remained outstanding at a weighted average exercise price of $2.40 per share.

The issuance of stock options and the common stock issuable upon the exercise of such options as described in this section (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with the Registrant’s employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about the Registrant or had access, through employment or other relationships, to such information.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued shares of common stock described in this Item 15 included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

Item 16. ***Exhibits and Financial Statement Schedules***

(a) Exhibits

Exhibit Number	Description
1.1*	Form of Underwriting Agreement.
3.1**	Restated Certificate of Incorporation of the Registrant.
3.2*	Form of Restated Certificate of Incorporation of the Registrant to be effective upon closing of the offering.
3.3**	Amended and Restated Bylaws of the Registrant.
3.4*	Form of Amended and Restated Bylaws of the Registrant to be effective upon the closing of the offering.
4.1*	Specimen Stock Certificate evidencing shares of common stock.
4.2**	Fifth Amended and Restated Investor Rights Agreement, dated as of September 21, 2005, by and among the Registrant and the other parties named therein.
4.3**	Warrant to Purchase Shares of Series C Convertible Preferred Stock, dated May 26, 2000, issued to Three Crowns Capital (Bermuda) Ltd.
4.4**	Warrant to Purchase Shares of Common Stock, dated March 15, 2001, issued to Silicon Valley Bank.
4.5**	Warrant to Purchase Shares of Series D Convertible Preferred Stock, dated August 17, 2001, issued to Three Crowns Capital (Bermuda) Ltd.
4.6**	Warrant to Purchase Shares of Series D Convertible Preferred Stock, dated August 28, 2001, issued to Three Crowns Capital (Bermuda) Ltd.
4.7**	Warrant to Purchase Shares of Series D Convertible Preferred Stock issued to General Electric Capital Corporation.
4.8**	Warrant to Purchase Shares of Common Stock, dated December 6, 2002, issued to Tularik Inc.
4.9**	Warrant to Purchase Shares of Series E Convertible Preferred Stock, dated December 19, 2003, issued to Three Crowns Capital (Bermuda) Ltd.
4.10**	Warrant to Purchase Shares of Series E Convertible Preferred Stock, dated April 21, 2004, issued Three Crowns Capital (Bermuda) Ltd.
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP.
10.1**	Sixth Amended and Restated 1998 Employee, Director and Consultant Stock Option Plan.
10.2*	2006 Equity and Long Term Incentive Plan.
10.3*	2006 Employee Stock Purchase Plan.
10.4┴**	Research Collaboration and Exclusive Option Agreement, dated as of December 1, 2005, by and between Bausch & Lomb Incorporated and the Registrant.
10.5┴**	Collaboration and License Agreement, dated as of March 17, 2006, by and between the Registrant and Essex Chemie AG, a wholly owned subsidiary of Schering-Plough Corporation.
10.6*	Employment Agreement, dated as of August 1, 2002, between the Registrant and Stuart W. Peltz, Ph.D.
10.7*	Executive Employment Agreement, dated as of December 15, 2004, between the Registrant and William D. Ju, M.D.
10.8*	Executive Employment Agreement, dated as of December 15, 2004, between the Registrant and Langdon Miller, M.D.
10.9*	Executive Employment Agreement, dated as of December 15, 2004, between the Registrant and William Baird, III.
10.10*	Executive Employment Agreement, dated as of December 15, 2004, between the Registrant and John Babiak, Ph.D.
10.11*	Executive Employment Agreement, dated as of December 15, 2004, between the Registrant and Mark E. Boulding.
10.12**	Lease Agreement, dated July 14, 2000, between the Registrant and 46.24 Associates L.P., as amended.
10.13**	Master Security Agreement, dated as of July 30, 2004, between the Registrant and Oxford Finance Corporation.

Exhibit Number	Description
10.14**	Form of Promissory Note issued to Oxford Finance Corporation.
23.1	Consent of KPMG LLP.
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1).
24.1**	Powers of Attorney (included on signature page).

* To be filed by amendment.
** Previously filed.
⊥ Confidential treatment requested as to portions of the exhibit. Confidential portions omitted and filed separately with the Securities and Exchange Commission.

(b) Financial Statement Schedules

All schedules have been omitted because they are not required or are not applicable or the required information is shown in the financial statements or notes thereto.

Item 17. ***Undertakings***

(a) The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the Underwriting Agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

(b) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the provisions described under Item 14 above, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

(c) The undersigned Registrant hereby undertakes that:

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

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

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this Amendment to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South Plainfield, New Jersey on the 4th day of May, 2006.

PTC THERAPEUTICS, INC.

By: /s/ STUART W. PELTZ

Stuart W. Peltz, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act, this Amendment to the Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ STUART W. PELTZ Stuart W. Peltz, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	May 4, 2006
/s/ WILLIAM BAIRD, III William Baird, III	Chief Financial Officer (Principal Financial and Accounting Officer)	May 4, 2006
* Michael Schmertzler	Chairman of the Board of Directors	May 4, 2006
* Harvey Berger, M.D.	Director	May 4, 2006
* Axel Bolte	Director	May 4, 2006
*ø Søren Carlsen, Ph.D.	Director	May 4, 2006
* Carl Goldfischer, M.D.	Director	May 4, 2006
* Allan Jacobson, Ph.D.	Director	May 4, 2006
* Michael Kranda	Director	May 4, 2006
* David P. Southwell	Director	May 4, 2006

*By: /s/ WILLIAM BAIRD, III
William Baird, III
Attorney-in-Fact

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24.1**	Powers of Attorney (included on signature page).

* To be filed by amendment.
** Previously filed.
⊥ Confidential treatment requested as to portions of the exhibit. Confidential portions omitted and filed separately with the Securities and Exchange Commission.

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
PTC Therapeutics, Inc:

We consent to the use of our report dated March 31, 2006 with respect to the balance sheets of PTC Therapeutics, Inc. as of December 31, 2004 and 2005, and the related statements of operations, stockholders' equity (deficit) and comprehensive loss, and cash flows for each of the years for the three-year period ended December 31, 2005 and for the period from March 31, 1998 (inception) to December 31, 2005, included herein and to the reference to our firm under the headings "Selected Financial Data" and "Experts" in the prospectus.

/s/ KPMG LLP

Philadelphia, Pennsylvania
May 3, 2006