

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

**AMENDMENT NO. 4 TO
FORM S-1
REGISTRATION STATEMENT**

*Under
The Securities Act of 1933*

THRESHOLD PHARMACEUTICALS, INC.

(Exact Name of Corporation as Specified in Its Charter)

	1300 Seaport Boulevard Redwood City, California 94063 (Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)	
	2834 (Primary Standard Industrial Classification Code Number)	94-3409596 (I.R.S. Employer Identification No.)
Delaware (State or other jurisdiction of incorporation or organization)		

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APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC: As soon as practicable after this registration statement becomes effective.

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

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

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

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

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Prices	Amount of Registration Fee(1)
Shares of Common Stock, par value \$0.001 per share	\$86,250,000	\$10,927.88

(1) Amount previously paid.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), 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 is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PROSPECTUS

SUBJECT TO COMPLETION, DATED DECEMBER 29, 2004



THRESHOLD PHARMACEUTICALS, INC.

COMMON STOCK

Threshold Pharmaceuticals, Inc. is offering _____ shares of common stock in a firmly underwritten offering. 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. After the offering, the market price for our shares may be outside this range.

We have applied to list our common stock on the NASDAQ National Market under the symbol "THLD."

Investing in our common stock involves a high degree of risk. See "[Risk Factors](#)" beginning on page 7.

	Per Share	Total
Offering price	\$ _____	\$ _____
Underwriting discounts and commissions	\$ _____	\$ _____
Proceeds to Threshold Pharmaceuticals, Inc., before offering costs	\$ _____	\$ _____

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

We have granted the underwriters an option to purchase up to _____ additional shares of our common stock to cover over-allotments, if any, within 30 days from the date of this prospectus. The underwriters expect to deliver the shares of common stock to our investors on or about _____, 2005.

Banc of America Securities LLC

CIBC World Markets

Lazard

William Blair & Company

_____, 2005

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You should rely only on the information contained in this prospectus. We have not, and the underwriters have not, authorized anyone to provide you with different information. We are not making an offer of these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus is accurate as of the date on the front of this prospectus only. Our business, financial condition, results of operations and prospects may have changed since that date.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus that we believe is most important to understanding how our business is currently being conducted. You should read the entire prospectus before making an investment decision.

Overview

We are a biotechnology company focused on the discovery, development and commercialization of drugs based on Metabolic Targeting™, an approach that targets fundamental differences in metabolism between normal and certain diseased cells. We are building a pipeline of drugs that are designed to selectively target tumor cells so that the drugs are less toxic to healthy tissues than conventional drugs, thereby providing improvements over current therapies.

Our initial clinical focus is the treatment of cancer and benign prostatic hyperplasia, or BPH, a disease characterized by overgrowth of the prostate. We have three product candidates. Glufosfamide, our lead product candidate for cancer, has completed Phase 1 and Phase 2 clinical trials in patients with various solid tumors. In September 2004, we initiated a pivotal Phase 3 clinical trial of glufosfamide for the second-line treatment of pancreatic cancer. We have received a special protocol assessment from the United States Food and Drug Administration, or FDA, for this trial. The special protocol assessment is a process that allows for official FDA evaluation of the proposed design of a Phase 3 clinical trial. It provides trial sponsors with an agreement from the FDA on trial design and analysis required to support a new drug application submission, if the study is performed according to the special protocol assessment and meets its primary endpoint. A primary end point is the measurement for determining the effectiveness of a drug candidate in treating the intended illness. In addition, glufosfamide for the treatment of refractory pancreatic cancer has received FDA fast track designation. The fast track drug development program provides for expedited regulatory review for new drugs demonstrating the potential to address unmet medical needs for the treatment of serious life-threatening conditions. TH-070, our lead product candidate for the treatment of symptomatic BPH, has completed enrollment in a Phase 2 clinical trial, and we are evaluating interim data. We plan to initiate a registrational program for TH-070 to treat symptomatic BPH in the first half of 2005. A registrational program is an overall plan for necessary information gathering and product testing, collectively designed to support ultimate market approval. Our third product candidate, 2-deoxyglucose, or 2DG, for the treatment of solid tumors, is being evaluated in a Phase 1 clinical trial as a combination therapy, which means that it is administered in conjunction with other chemotherapy treatments. We are also working to discover drug candidates that are activated under the metabolic conditions typical of cancer cells, and we have identified lead compounds with promising *in vitro* data. In addition, we are investigating additional compounds for activity against BPH.

Metabolic Targeting

Metabolic Targeting is a therapeutic approach that targets fundamental differences in energy metabolism between normal and certain diseased cells. To survive, these diseased cells rely predominantly on glycolysis, also called glucose metabolism, which is the process by which glucose is converted to energy. As a consequence, these cells consume more glucose than do normal cells. In cancer, this increased consumption of glucose has two causes: the process of a normal cell becoming a rapidly dividing cancer cell; and the exposure of a cell to the low oxygen conditions, also called hypoxia, within those regions of most solid tumors where cells are dividing slowly. When these cells shift energy production to glycolysis, they must increase the levels of the proteins needed to transport and metabolize glucose. Similarly, cells in BPH rely predominantly on glycolysis for energy production. Metabolic Targeting takes advantage of these metabolic differences to selectively target these diseased cells.

For the treatment of cancer, we believe that our product candidates based on Metabolic Targeting can be broadly applied to the treatment of most solid tumors and have the potential to significantly increase the effectiveness of existing therapies. Metabolic Targeting provides the opportunity to treat not only rapidly

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dividing tumor cells, which are targeted by chemotherapy and radiation, but also slowly dividing tumor cells that generally evade these traditional therapies and ultimately contribute to relapse. For the treatment of BPH, we believe that Metabolic Targeting will enable us to develop a new class of drugs to treat the disease more rapidly and effectively, with fewer side effects than current therapies. We believe that our focus on Metabolic Targeting, combined with our expertise in medicinal chemistry and drug development, provides us with the capability to identify, discover and develop novel therapies.

Glufosfamide

Glufosfamide, our lead product candidate for cancer, is a small molecule in clinical development for the treatment of pancreatic cancer. We are developing glufosfamide as an intravenous single agent for the second-line treatment of metastatic pancreatic cancer, and in combination with Gemzar® (gemcitabine) for the first-line treatment of inoperable locally advanced or metastatic pancreatic cancer. Gemzar, a patented drug marketed by Lilly, is currently the standard of care for treatment of pancreatic cancer. First-line treatment means the patient has not been previously treated with chemotherapy. Second-line treatment means the patient has been previously treated with one regimen of chemotherapy.

In September 2004, we initiated a pivotal Phase 3 trial of glufosfamide for the treatment of patients with metastatic pancreatic cancer who have failed treatment with Gemzar. This trial will compare the survival of patients treated with glufosfamide to patients who receive only best supportive care. The FDA has completed a special protocol assessment for this trial and concluded that the trial design and analysis would support a new drug application submission if the study is performed according to the special protocol assessment and the trial meets its primary endpoint by demonstrating a statistically significant effect on patient survival. In addition, glufosfamide for the treatment of refractory pancreatic cancer has been granted fast track designation by the FDA. The fast track drug development program provides for expedited regulatory review for new drugs demonstrating the potential to address unmet medical needs for the treatment of serious or life-threatening conditions. As part of our registration and approval strategy, in December 2004, we initiated a Phase 1/2 trial to evaluate various doses of glufosfamide in combination with Gemzar for the first-line treatment of advanced pancreatic cancer patients. We are developing glufosfamide for pancreatic cancer based on activity seen in previous clinical trials, a known increase in glucose uptake in pancreatic cancer cells and the extreme hypoxia in tumors of this type.

Glufosfamide has been evaluated in two Phase 1 and five Phase 2 clinical trials that together enrolled over 200 patients with a variety of advanced-stage cancers. In the Phase 2 trials, glufosfamide showed activity against breast, colon, non-small cell lung and pancreatic cancers, but not a type of brain cancer called glioblastoma. In a 34-patient Phase 2 trial of patients with advanced pancreatic cancer, overall median survival with glufosfamide was estimated at 5.6 months, and two-year survival was estimated at 9%. In the Phase 1 and Phase 2 trials, glufosfamide was generally well tolerated, with few drug-related serious adverse events. The safety and efficacy of glufosfamide to treat pancreatic cancer will need to be demonstrated in our pivotal Phase 3 program before we can receive marketing approval from the FDA or foreign regulatory agencies.

TH-070

TH-070, our lead product candidate for the treatment of symptomatic BPH, is in a Phase 2 trial in Italy. The primary objective of this trial is to determine the safety and tolerability of TH-070 in patients with BPH. In addition, patients are being evaluated for efficacy as measured by changes in specific variables that have been used in clinical trials of currently marketed BPH drugs to support their FDA approval. The primary endpoint specified in the protocol for our trial is a comparison of prostate size between baseline and day 28 of treatment. We have completed enrollment and are evaluating 14-day and 28-day interim data. Interim data are preliminary results from a predetermined portion of study participants. We observed statistically significant improvements in all variables measured by day 14, and further improvements by day 28. In the study, TH-070 was well tolerated with no therapy-related side effects. The safety and efficacy of TH-070 for the treatment of symptomatic BPH will need to be demonstrated in subsequent trials. Based on these interim Phase 2 results, we are designing a registrational program for TH-070 to treat symptomatic BPH. We expect to commence two clinical trials in the

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first half of 2005, at least one of which will be a Phase 3 trial. There can be no assurance that regulatory agencies will consider these studies pivotal, and we expect our registration program to include additional trials.

TH-070 is an orally administered small molecule that has been reported to inhibit the enzyme that catalyzes the first step in glycolysis. We initially selected TH-070 to treat BPH based on our understanding that prostate cells rely predominantly on glycolysis for energy production as well as published animal data and human clinical data demonstrating tolerability.

TH-070 offers the potential to treat symptomatic BPH via a novel mechanism, by reducing the prostate size through Metabolic Targeting. By directly inhibiting glycolysis in prostate cells, we expect TH-070 to reduce the size of the prostate more rapidly than current medical treatments, without the attendant side effects, which include decreased libido, impotence and cardiovascular effects.

2-Deoxyglucose (2DG)

2DG, our product candidate for the treatment of solid tumors, is in a Phase 1 trial. 2DG is an orally administered small molecule that employs Metabolic Targeting to treat solid tumors by directly inhibiting glycolysis, the major source of energy production in these tissues. Because tumor cells in general, and those in hypoxic zones in particular, are dependent on glycolysis for survival, tumor cells are particularly sensitive to the effect of 2DG. We are conducting a Phase 1 trial of daily 2DG as a single agent and in combination with Taxotere[®] (docetaxel) to evaluate the safety, blood levels and maximum tolerated dose of 2DG in patients with solid tumors. Taxotere, a patented drug marketed by the sanofi-aventis Group, is used to treat different types of cancer, including lung and breast cancers. We plan to conduct a Phase 1 trial of a single dose of 2DG to evaluate its effect on prostate metabolism. We are developing 2DG based on its specificity for targeting tumor cells and extensive human safety data, as well as recently demonstrated animal efficacy that we and our collaborators published in *Cancer Research* in January 2004.

Our Strategy

Our goal is to create a leading biotechnology company that develops and commercializes drugs based on Metabolic Targeting, with an initial focus on cancer and BPH. Key elements of our strategy are to:

- Develop glufosfamide, TH-070 and 2DG successfully;
- Continue to broaden our pipeline by identifying, discovering and developing new compounds;
- Build on our expertise in Metabolic Targeting through continued research in cellular metabolism; and
- Develop sales and marketing capabilities in select markets.

In executing our business strategy, we face significant risks and uncertainties, which are highlighted in the section entitled “Risk Factors.” We are a development stage company and have a limited operating history. We have experienced operating losses since our inception, and we expect to incur significantly greater operating losses for the next several years as we advance our clinical development programs. None of our product candidates has been approved for sale by the FDA, and we have not generated any revenue since our inception. If we are unable to develop, receive regulatory approval for and successfully commercialize any of our product candidates, we will be unable to generate significant revenues, and we may never become profitable.

Our Corporate Information

We were incorporated in Delaware on October 17, 2001. Our principal executive offices are located at 1300 Seaport Boulevard, Redwood City, California, 94063. Our telephone number is (650) 474-8200. Our website is located at www.thresholdpharm.com. Information contained on, or that can be accessed through, our website is not part of this prospectus.

Unless the context requires otherwise, in this prospectus the terms “Threshold Pharmaceuticals,” “we,” “us” and “our” refer to Threshold Pharmaceuticals, Inc. Threshold Pharmaceuticals, Inc., our logo and Metabolic Targeting are our trademarks. Other trademarks, trade names and service marks used in this prospectus are the property of their respective owners.

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THE OFFERING

Common stock offered	shares
Common stock to be outstanding after the offering	shares
Use of proceeds	We intend to use the net proceeds from this offering for clinical development of our glufosfamide, TH-070 and 2DG product candidates, research and development activities, initial development of sales and marketing infrastructure and working capital and other general corporate purposes. See “Use of Proceeds” for additional information.
Risk Factors	See “Risk Factors” and the other information in this prospectus for important information that you should consider before deciding whether to invest in shares of our common stock.
Proposed NASDAQ National Market symbol	THLD

The number of shares of our common stock to be outstanding after the closing of this offering is based on 5,548,047 shares of our common stock outstanding as of September 30, 2004 and has been adjusted to reflect, and unless otherwise indicated, the conversion of all of our outstanding preferred stock into 33,848,484 shares of our common stock, which will occur automatically upon the closing of this offering.

The number of shares of our common stock outstanding after the offering excludes:

- 437,000 shares of our common stock that were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 423,231 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2004 at a weighted average exercise price of \$0.24 per share;
- 38,000 shares of common stock issuable upon exercise of a warrant outstanding as of September 30, 2004 with an exercise price of \$1.00 per share, which does not expire upon the closing of this offering;
- 879,222 shares of common stock available for future grants under our 2001 Stock Option Plan as of September 30, 2004;
- 4,000,000 shares of common stock reserved for issuance under our 2004 Equity Incentive Plan; and
- shares of common stock reserved for issuance under our 2004 Employee Stock Purchase Plan.

Unless otherwise indicated, all information in this prospectus assumes that the underwriters do not exercise their option to purchase up to shares of our common stock to cover over-allotments, if any, and 33,848,484 shares of our common stock resulting from the conversion of all outstanding shares of our preferred stock into common stock upon completion of this offering.

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SUMMARY FINANCIAL DATA

The summary financial data set forth below should be read in conjunction with our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus. See Note 2 to our financial statements for information regarding computation of net loss per share attributable to common stockholders and Note 13 to our financial statements for information regarding computation of pro forma net loss per share attributable to common stockholders.

	Period from October 17, 2001 (date of inception) to December 31, 2001	Years Ended December 31,		Nine Months Ended September 30,		Cumulative Period from October 17, 2001 (date of inception) to September 30, 2004
		2002	2003	2003	2004	
(In thousands, except per share data)						
Operating expenses:						
Research and development	\$ 35	\$ 2,179	\$ 6,252	\$ 4,868	\$ 10,852	\$ 19,318
General and administrative	201	306	2,057	1,591	5,137	7,701
Total operating expenses	236	2,485	8,309	6,459	15,989	27,019
Loss from operations	(236)	(2,485)	(8,309)	(6,459)	(15,989)	(27,019)
Interest income	—	27	65	17	313	405
Interest expense	—	—	(59)	(24)	(27)	(86)
Net loss	(236)	(2,458)	(8,303)	(6,466)	(15,703)	(26,700)
Dividend related to beneficial conversion feature of convertible preferred stock	—	—	(40,862)	—	—	(40,862)
Net loss attributable to common stockholders	\$ (236)	\$ (2,458)	\$ (49,165)	\$ (6,466)	\$ (15,703)	\$ (67,562)
Net loss per common share:						
Basic and diluted	\$ (1.29)	\$ (21.19)	\$ (305.37)	\$ (40.92)	\$ (16.14)	
Weighted average number of shares used in per common share calculations:						
Basic and diluted	183	116	161	158	973	
Pro forma net loss per common share (unaudited):						
Basic and diluted ⁽¹⁾			\$ (4.04)		\$ (0.45)	
Weighted average number of shares used in pro forma per common share calculations (unaudited):						
Basic and diluted			12,156		34,821	

(1) Pro forma basic and diluted net loss per common share have been computed to give effect to the automatic conversion of all of our outstanding preferred stock into 33,848,484 shares of common stock upon the closing of this offering (using the as-converted method) for the year ended December 31, 2003 and for the nine months ended September 30, 2004.

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The following table presents a summary of our balance sheet as of September 30, 2004:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all of our outstanding preferred stock into 33,848,484 shares of our common stock upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale of shares of common stock by us in this offering at an assumed initial public offering price of \$ _____ per share (the midpoint of the estimated price range shown on the cover page of this prospectus), after deducting underwriting discounts and commissions and estimated offering costs to be paid by us.

	As of September 30, 2004		
	Actual	Pro Forma	Pro Forma As Adjusted
	(In thousands)		
Balance Sheet Data:			
Cash and cash equivalents	\$ 16,237	\$ 16,237	\$
Working capital	28,587	28,587	
Total assets	31,375	31,375	
Notes payable, less current portion	185	185	
Redeemable convertible preferred stock	49,839	—	
Total stockholders' equity (deficit)	(20,940)	28,899	

RISK FACTORS

Any investment in our stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below and all information contained in this prospectus, before you decide whether to purchase our common stock. The trading price of our common stock could decline due to any of these risks or uncertainties, and you may lose part or all of your investment.

RISKS RELATED TO OUR BUSINESS

Risks Related to Drug Discovery, Development and Commercialization

We are substantially dependent upon the success of our glufosfamide and TH-070 product candidates. Pivotal clinical trials for our products may not demonstrate efficacy or lead to regulatory approval.

We will not be able to commercialize our lead product candidates, glufosfamide and TH-070, until we obtain FDA approval in the United States or approval by comparable regulatory agencies in Europe and other countries. To satisfy FDA or foreign regulatory approval standards for the commercial sale of our product candidates, we must demonstrate in adequate and controlled clinical trials that our product candidates are safe and effective. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. For example, estimates of survival time or percentages obtained from small scale Phase 2 clinical trials are not necessarily indicative of the results in larger clinical trials.

Phase 1 and Phase 2 safety trials of glufosfamide were conducted on small numbers of patients and were designed to evaluate the activity of glufosfamide on a preliminary basis. However, these trials were not designed to demonstrate the efficacy of glufosfamide as a therapeutic agent. Although we believe the Phase 1 and Phase 2 trials of glufosfamide have generated promising early data, there can be no assurance that similar results will be observed in subsequent trials, or that such results will prove to be statistically significant or demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory agencies. In Phase 2 studies, glufosfamide has not shown clinical activity for the treatment of glioblastoma and has only demonstrated marginal activity for the treatment of non-small cell lung cancer. We believe that the clinical trial we commenced in September 2004 for the second-line treatment of pancreatic cancer will serve as a pivotal Phase 3 trial. If the results from this trial are not persuasive as determined by the FDA, then this trial will not serve as the basis for FDA approval. Even though we have a special protocol assessment for this trial, we may decide to conduct additional clinical trials or other studies, or the FDA may require us to conduct additional clinical trials or other studies prior to accepting our NDA or granting marketing approval.

While we believe that interim results of our Phase 2 trial for TH-070 suggest it may effectively treat symptomatic BPH, there can be no assurance that our registrational program will confirm our interim results, will show that beneficial results of TH-070 will be sustained beyond 28 days, or will lead to regulatory approval. Moreover, regulatory agencies may require additional preclinical and clinical studies to support approval of TH-070 for the treatment of symptomatic BPH. The clinical trials we plan to commence in 2005 for TH-070 may not be pivotal trials.

Our product candidates must undergo rigorous clinical testing, the results of which are uncertain and could substantially delay or prevent us from bringing them to market.

Before we can obtain regulatory approval for a product candidate, we must undertake extensive clinical testing in humans to demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory agencies. Clinical trials of new drug candidates sufficient to obtain regulatory marketing approval are expensive and take years to complete.

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We cannot assure you that we will successfully complete clinical testing within the time frame we have planned, or at all. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our product candidates, including the following:

- our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and/or preclinical testing or to abandon programs;
- the results obtained in earlier stage testing may not be indicative of results in future trials;
- trial results may not meet the level of statistical significance required by the FDA or other regulatory agencies;
- enrollment in our clinical trials for our product candidates may be slower than we anticipate, resulting in significant delays;
- we, or regulators, may suspend or terminate our clinical trials if the participating patients are being exposed to unacceptable health risks; and
- the effects of our product candidates on patients may not be the desired effects or may include undesirable side effects or other characteristics that may delay or preclude regulatory approval or limit their commercial use, if approved.

Completion of clinical trials depends, among other things, on our ability to enroll a sufficient number of patients, which is a function of many factors, including:

- the therapeutic endpoints chosen for evaluation;
- the eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's therapeutic endpoints;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents; and
- competition for patients by clinical trial programs for other treatments.

We may experience difficulties in enrolling patients in our clinical trials, which could increase the costs or affect the timing or outcome of these trials. This is particularly true with respect to diseases with relatively small patient populations, such as pancreatic cancer, which is an indication for our glufosfamide product candidate.

We are subject to significant regulatory approval requirements, which could delay, prevent or limit our ability to market our product candidates.

Our research and development activities, preclinical studies, clinical trials and the anticipated manufacturing and marketing of our product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in Europe and elsewhere. We require the approval of the relevant regulatory authorities before we may commence commercial sales of our product candidates in a given market. The regulatory approval process is expensive and time-consuming, and the timing of receipt of regulatory approval is difficult to predict. Our product candidates could require a significantly longer time to gain regulatory approval than expected, or may never gain approval. We cannot assure you that, even after expending substantial time and financial resources, we will obtain regulatory approval for any of our product candidates. A delay or denial of regulatory approval could delay or prevent our ability to generate product revenues and to achieve profitability.

Changes in the regulatory approval policy during the development period of any of our product candidates, changes in, or the enactment of, additional regulations or statutes, or changes in regulatory review practices for a submitted product application may cause a delay in obtaining approval or result in the rejection of an application for regulatory approval.

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Regulatory approval, if obtained, may be made subject to limitations on the indicated uses for which we may market a product. These limitations could adversely affect our potential product revenues. Regulatory approval may also require costly post-marketing follow-up studies. In addition, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping related to the product will be subject to extensive ongoing regulatory requirements. Furthermore, for any marketed product, its manufacturer and its manufacturing facilities will be subject to continual review and periodic inspections by the FDA or other regulatory authorities. Failure to comply with applicable regulatory requirements may, among other things, result in fines, suspensions of regulatory approvals, product recalls, product seizures, operating restrictions and criminal prosecution.

The “fast track” designation for development of glufosfamide for the treatment of refractory pancreatic cancer may not 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 for a particular indication. Marketing applications filed by sponsors of products in fast track development may qualify for expedited FDA review under the policies and procedures offered by the FDA, but the fast track designation does not assure any such qualification. Although we have obtained a fast track designation from the FDA for glufosfamide for the treatment of refractory pancreatic cancer, we may not experience a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures. In addition, the FDA may withdraw our fast track designation at any time. If we lose our fast track designation, the approval process may be delayed. In addition, our fast track designation does not guarantee that we will qualify for or be able to take advantage of the expedited review procedures and does not increase the likelihood that glufosfamide will receive regulatory approval for the treatment of refractory pancreatic cancer.

Our product candidates are based on Metabolic Targeting, which is an unproven approach to therapeutic intervention.

All of our product candidates are based on Metabolic Targeting, a therapeutic approach that targets fundamental differences in energy metabolism between normal and certain diseased cells. We have not, nor to our knowledge has any other company, received regulatory approval for a drug based on this approach. There can be no assurance that our approach will lead to the development of approvable or marketable drugs.

In addition, the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of drugs based on Metabolic Targeting, which could lengthen the regulatory review process, increase our development costs and delay or prevent commercialization of our product candidates.

Our product candidates may have undesirable side effects that prevent their regulatory approval or limit their use if approved.

Glufosfamide is known to cause reversible toxicity to the bone marrow and kidneys, as well as nausea and vomiting. TH-070, which we are developing to treat patients with BPH, has been investigated in clinical studies as a male contraceptive and is known to cause reversible testicular pain in some patients. These side effects or others that could be identified in the course of our clinical trials or that may otherwise be associated with our product candidates may outweigh the benefits of our product candidates and prevent regulatory approval or limit their market acceptance if they are approved.

Delays in clinical testing could result in increased costs to us and delay our ability to obtain regulatory approval and commercialize our product candidates.

Significant delays in clinical testing could materially impact our product development costs and delay regulatory approval of our product candidates. We do not know whether planned clinical trials will begin on

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time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in:

- obtaining regulatory approval to commence a trial;
- obtaining clinical materials;
- reaching agreement on acceptable clinical study agreement terms with prospective sites;
- obtaining institutional review board approval to conduct a study at a prospective site; and
- recruiting patients to participate in a study.

Orphan drug exclusivity affords us limited protection, and if another party obtains orphan drug exclusivity for the drugs and indications we are targeting, we may be precluded from commercializing our product candidates in those indications.

We intend to seek orphan drug designation for the cancer indications that our glufosfamide and 2DG product candidates are intended to treat. Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is defined by the FDA as a disease or condition that affects fewer than 200,000 individuals in the United States. The company that obtains the first FDA approval for a designated orphan drug indication receives marketing exclusivity for use of that drug for that indication for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug. Orphan drug designation does not shorten the development or regulatory review time of a drug, but does provide limited advantages in the regulatory review and approval process. Because the prevalence of BPH is greater than 200,000 individuals in the United States, TH-070 for the treatment of symptomatic BPH is not eligible for orphan drug designation and we cannot rely on this protection to provide marketing exclusivity.

Orphan drug exclusivity may not prevent other market entrants. A different drug, or, under limited circumstances, the same drug may be approved by the FDA for the same orphan indication. The limited circumstances are an inability to supply the drug in sufficient quantities or where a new formulation of the drug has shown superior safety or efficacy. As a result, if our product is approved and receives orphan drug status, the FDA can still approve other drugs for use in treating the same indication covered by our product, which could create a more competitive market for us.

Moreover, due to the uncertainties associated with developing pharmaceutical products, we may not be the first to obtain marketing approval for any orphan drug indication. Even if we obtain orphan drug designation, if a competitor obtains regulatory approval for glufosfamide or 2DG for the same indication we are targeting before us, we would be blocked from obtaining approval for that indication for seven years, unless our product is a new formulation of the drug that has shown superior safety or efficacy, or the competitor is unable to supply sufficient quantities.

Even if we obtain regulatory approval, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing United States and foreign regulations, we could lose our approvals to market drugs and our business would be seriously harmed.

Following initial regulatory approval of any drugs we may develop, we will be subject to continuing regulatory review, including review of adverse drug experiences and clinical results that are reported after our drug products become commercially available. This would include results from any post-marketing tests or vigilance required as a condition of approval. The manufacturer and manufacturing facilities we use to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. If a previously unknown problem or problems with a product or a manufacturing and laboratory facility used by us is discovered, the FDA or foreign regulatory agency may impose restrictions on that product or on the manufacturing facility, including requiring us to withdraw the product from the market. Any changes to an

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approved product, including the way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our contract manufacturers will be subject to ongoing FDA requirements for submission of safety and other post-market information. If we and our contract manufacturers fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw our regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on our operations;
- close the facilities of our contract manufacturers; or
- seize or detain products or require a product recall.

Risks Related to Our Financial Performance and Operations

We have incurred losses since our inception and anticipate that we will incur significant continued losses for the next several years, and our future profitability is uncertain.

We are a development stage company with a limited operating history and no current source of revenue from our product candidates. We have incurred losses in each year since our inception in 2001. We have devoted substantially all of our resources to research and development of our product candidates. We have financed our operations primarily through private placements of our equity securities. For the year ended December 31, 2003, we had a net loss of \$8.3 million and for the nine months ended September 30, 2004, we had a net loss of \$15.7 million. As of September 30, 2004, we had an accumulated deficit of \$26.7 million. We do not expect to generate any revenue from our product candidates over the next several years. Clinical trials are costly, and as we continue to advance our product candidates through development, we expect our research and development expenses to increase significantly, especially as we continue our pivotal Phase 3 clinical trial for glufosfamide and begin our registrational program for TH-070 for the treatment of BPH. In addition, we plan to significantly expand our operations, and will need to expand our infrastructure and facilities and hire additional personnel. As a result, we expect that our annual operating losses will increase significantly over the next several years.

To attain profitability, we will need to successfully develop products and effectively market and sell them. We have never generated revenue from our product candidates, and there is no guarantee that we will be able to do so in the future. If our glufosfamide or TH-070 product candidates fail to show positive results in our ongoing clinical trials, and we do not receive regulatory approval for one or more of them, or if these product candidates do not achieve market acceptance even if approved, we will not become profitable for at least the next several years. If we fail to become profitable, or if we are unable to fund our continuing losses, we may be unable to continue our clinical development programs, and you could lose your entire investment.

We may need substantial additional funding and may be unable to raise capital when needed, which could force us to delay, reduce or eliminate our drug discovery, product development and commercialization activities.

Developing drugs, conducting clinical trials, and commercializing products is expensive. Our future funding requirements will depend on many factors, including:

- the progress and cost of our clinical trials and other research and development activities;
- the costs and timing of obtaining regulatory approval;

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- the costs of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights;
- the cost and timing of securing manufacturing capabilities for our clinical product candidates and commercial products, if any;
- the costs of establishing sales, marketing and distribution capabilities; and
- the terms and timing of any collaborative, licensing and other arrangements that we may establish.

We believe that the net proceeds from this offering, together with our cash on hand, will be sufficient to fund our projected operating requirements for at least the next two years, including clinical trials of glufosfamide, TH-070 and 2DG, the initial development of a sales and marketing effort, general corporate purposes and for the research and development of additional product candidates. However, we may need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic and market conditions and other factors, many of which are beyond our control. There can be no assurance that sufficient funds will be available to us when required or on satisfactory terms. If necessary funds are not available, we may have to delay, reduce the scope or eliminate some of our development programs, which could delay the time to market for any of our product candidates. We may also need to seek funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Raising additional funds may cause dilution to existing stockholders or require us to relinquish valuable rights.

We may raise additional funds through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience further dilution. Debt financing, if available, may subject us to restrictive covenants that could limit our flexibility in conducting future business activities. To the extent that we raise additional funds through collaboration and licensing arrangements, it will be necessary to relinquish some rights to our clinical product candidates.

If we are unable to establish sales and marketing capabilities, we may be unable to successfully commercialize our cancer and BPH product candidates.

If our cancer product candidates are approved for commercial sale, we plan to establish our own sales force to market them in the United States and potentially Europe. We may also consider establishing a sales force to market TH-070 for the treatment of symptomatic BPH. We currently have no experience in selling, marketing or distributing pharmaceutical products and do not have a sales force to do so. Before we can commercialize any products, we must develop our sales, marketing and distribution capabilities, which is an expensive and time consuming process, and our failure to do this successfully could delay any product launch. Our efforts to develop internal sales and marketing capabilities could face a number of risks, including:

- we may not be able to attract a sufficient number of qualified sales and marketing personnel;
- the cost of establishing a marketing or sales force may not be justifiable in light of the potential revenues for any particular product; and
- our internal sales and marketing efforts may not be effective.

Our success depends in part on recruiting and retaining key personnel and, if we fail to do so, it may be more difficult for us to execute our business strategy. We are currently a small organization and will need to hire additional personnel to execute our business strategy successfully.

Our success depends on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel and on our ability to develop and maintain important relationships with leading

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academic institutions, clinicians and scientists. We are highly dependent upon our senior management and scientific staff, particularly our Chief Executive Officer, Dr. Harold E. Selick, and our founder and President, Dr. George F. Tidmarsh. We do not have employment contracts with either Dr. Selick or Dr. Tidmarsh. We are named as the beneficiary on term life insurance policies covering Dr. Selick and Dr. Tidmarsh in the amount of \$2 million each. The loss of the services of Dr. Selick, Dr. Tidmarsh or one or more of our other key employees could delay or prevent the successful completion of our clinical trials or the commercialization of our product candidates.

As of November 30, 2004, we had 42 employees. Over the next three to six months, we expect to add a significant number of new employees at an annual cost between \$2 and \$4 million. Our success will depend on our ability to hire additional qualified personnel. Competition for qualified personnel in the biotechnology field is intense. We face competition for personnel from other biotechnology and pharmaceutical companies, universities, public and private research institutions and other organizations. We may not be able to attract and retain qualified personnel on acceptable terms given the competition for such personnel. If we are unsuccessful in our recruitment efforts, we may be unable to execute our strategy.

As we expand our operations, we may experience difficulties in managing our growth.

Future growth will impose significant added responsibilities on management, including the need to identify, recruit, train and integrate additional employees. In addition, rapid and significant growth will place a strain on our administrative and operational infrastructure. As our operations expand, we expect that we will need to manage additional relationships with collaborators and various third parties, including contract research organizations, manufacturers and others. Our ability to manage our operations and growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. If we are unable to manage our growth effectively, it may be difficult for us to execute our business strategy.

Because we have operated as a private company, we have no experience complying with public company obligations, including recently enacted changes in securities laws and regulations. Compliance with these requirements will increase our costs and require additional management resources, and we still may fail to comply.

We are a small company with limited resources. We have operated as a private company, not subject to many of the requirements applicable to public companies. While we plan to expand our staff if we become public, we may encounter substantial difficulty attracting qualified staff with requisite experience due to the high level of competition for experienced financial professionals.

As directed by Section 404 of the Sarbanes-Oxley Act of 2002, the SEC adopted rules requiring public companies to include a report of management on the company's internal controls over financial reporting in their annual reports on Form 10-K. In addition, the independent registered public accounting firm auditing the company's financial statements must attest to and report on management's assessment of the effectiveness of the company's internal controls over financial reporting. This requirement will first apply to our annual report on Form 10-K for our fiscal year ending December 31, 2005. Substantial uncertainty exists regarding our ability to comply with these requirements by applicable deadlines. If we are unable to complete the required assessment as to the adequacy of our internal control reporting or if our independent registered public accounting firm is unable to provide us with an unqualified report as to the effectiveness of our internal controls over financial reporting as of December 31, 2005 and future year ends, investors could lose confidence in the reliability of our internal controls over financial reporting.

Our facilities in California are located near an earthquake fault, and an earthquake or other natural disaster or resource shortage could disrupt our operations.

Important documents and records, such as hard copies of our laboratory books and records for our product candidates, are located in our corporate headquarters at a single location in Redwood City, California, near active

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earthquake zones. In the event of a natural disaster, such as an earthquake, drought or flood, or localized extended outages of critical utilities or transportation systems, we do not have a formal business continuity or disaster recovery plan, and could therefore experience a significant business interruption. In addition, California from time to time has experienced shortages of water, electric power and natural gas. Future shortages and conservation measures could disrupt our operations and could result in additional expense. Although we maintain business interruption insurance coverage, the policy specifically excludes coverage for earthquake and flood.

Risks Related to Our Dependence on Third Parties

We rely on third parties to manufacture glufosfamide, TH-070 and 2DG. If these parties do not manufacture the active pharmaceutical ingredients or finished products of satisfactory quality, in a timely manner, in sufficient quantities or at an acceptable cost, clinical development and commercialization of our product candidates could be delayed.

We do not currently own or operate manufacturing facilities; consequently, we rely and expect to continue to rely on third parties for the production of clinical and commercial quantities of our product candidates. We have not yet entered into any long term manufacturing or supply agreement for any of our product candidates. Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our ability to develop and commercialize any product candidates on a timely and competitive basis.

Our current supplies of glufosfamide have been prepared by a subsidiary of Baxter International, Inc. and we are depending on those materials in order to conduct and complete our planned clinical trials. Should those materials not remain stable, we may experience a significant delay in the completion of our pivotal Phase 3 trial. Although we are in the process of qualifying back-up vendors to manufacture glufosfamide active pharmaceutical ingredient, or API, and drug product, we have not yet done so, and we may not be able to do so at an acceptable cost or terms, if at all.

We believe that we have sufficient supplies of TH-070 API to conduct and complete our currently planned BPH clinical trials. We have ordered additional TH-070 API from Jiangsu Hengrui Medicine Company, Ltd. We have recently entered into an agreement with Pharmaceutics International, Incorporated for the manufacture of TH-070 drug product. We have not yet received any API or drug product from these manufacturers. The failure of Pharmaceutics International to meet quality requirements or otherwise perform its obligations could significantly delay our TH-070 clinical program. In addition, failure of Jiangsu Hengrui Medicine Company to provide acceptable API could delay commercialization of TH-070, if approved.

We believe that we have a sufficient supply of 2DG for our anticipated clinical trials over the next two years, although there can be no assurance that these supplies will remain stable and usable during this period. If these materials are not stable, we may experience a significant delay in our 2DG clinical program.

We will need to enter into additional agreements for additional supplies of each of our product candidates to complete clinical development and/or commercialize them. There can be no assurance that we can do so on favorable terms, if at all. For regulatory purposes, we will have to demonstrate comparability of the same drug substance from different manufacturers. Our inability to do so could delay our clinical programs.

To date, our product candidates have been manufactured in quantities sufficient for preclinical studies or initial clinical trials. If any of our product candidates is approved by the FDA or other regulatory agencies for commercial sale, we will need to have it manufactured in commercial quantities. We may not be able to successfully increase the manufacturing capacity for any of our product candidates in a timely or economic manner or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA and other regulatory agencies must review and approve. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed, or there may be a shortage of supply which could limit our sales.

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In addition, if the facility or the equipment in the facility that produces our product candidates is significantly damaged or destroyed, or if the facility is located in another country and trade or commerce with such country is interrupted, we may be unable to replace the manufacturing capacity quickly or inexpensively. The inability to obtain manufacturing agreements, the damage or destruction of a facility on which we rely for manufacturing or any other delays in obtaining supply would delay or prevent us from completing our clinical trials and commercializing our current product candidates.

We have no control over our manufacturers' and suppliers' compliance with manufacturing regulations, and their failure to comply could result in an interruption in the supply of our product candidates.

The facilities used by our contract manufacturers must undergo an inspection by the FDA for compliance with current good manufacturing practice, or cGMP regulations, before the respective product candidates can be approved. In the event these facilities do not receive a satisfactory cGMP inspection for the manufacture of our product candidates, we may need to fund additional modifications to our manufacturing process, conduct additional validation studies, or find alternative manufacturing facilities, any of which would result in significant cost to us as well as a delay of up to several years in obtaining approval for such product candidate. In addition, our contract manufacturers, and any alternative contract manufacturer we may utilize, will be subject to ongoing periodic inspection by the FDA and corresponding state and foreign agencies for compliance with cGMP regulations and similar foreign standards. We do not have control over our contract manufacturers' compliance with these regulations and standards. Any failure by our third-party manufacturers or suppliers to comply with applicable regulations could result in sanctions being imposed on them (including fines, injunctions and 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 prosecution.

We rely on third parties to conduct our clinical trials, and their failure to perform their obligations in a timely or competent manner may delay development and commercialization of our product candidates.

We rely almost exclusively on third-party clinical investigators to conduct our clinical trials and other third-party organizations to oversee the operations of such clinical trials and to perform data collection and analysis. We are currently using several third-party clinical investigators. We are also using clinical research organizations to oversee our ongoing glufosfamide and TH-070 clinical trials and expect to use the same or similar organizations for our anticipated clinical trials. There are numerous alternative sources to provide these services. However, we may face delays outside of our control if these parties do not perform their obligations in a timely or competent fashion or if we are forced to change service providers. This risk is heightened for our clinical trials conducted outside of the United States, where it may be more difficult to ensure that studies are conducted in compliance with FDA requirements. We will rely significantly upon the accrual of patients at clinical sites outside the United States. Any third-party that we hire to conduct clinical trials may also provide services to our competitors, which could compromise the performance of their obligations to us. If we experience significant delays in the progress of our clinical trials and in our plans to file NDAs, the commercial prospects for product candidates could be harmed and our ability to generate product revenue would be delayed or prevented.

We may rely on strategic collaborators to market and sell TH-070 for the treatment of BPH worldwide and our potential cancer products outside the United States.

We have no sales and marketing experience. We may contract with strategic collaborators to sell and market TH-070 for the treatment of symptomatic BPH worldwide and our cancer products outside the United States. We may not be successful in entering into collaborative arrangements with third parties for the sale and marketing of any products. Any failure to enter into collaborative arrangements on favorable terms could delay or hinder our ability to develop and commercialize our product candidates and could increase our costs of development and commercialization. Dependence on collaborative arrangements will subject us to a number of risks, including:

- we may not be able to control the amount or timing of resources that our collaborators may devote to the product candidates;

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- we may be required to relinquish important rights, including intellectual property, marketing and distribution rights;
- we may have lower revenues than if we were to market and distribute such products ourselves;
- should a collaborator fail to commercialize one of our product candidates successfully, we may not receive future milestone payments or royalties;
- a collaborator could separately move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors;
- our collaborators may experience financial difficulties;
- business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement; and
- our collaborators may operate in countries where their operations could be adversely affected by changes in the local regulatory environment or by political unrest.

Risks Related to Our Intellectual Property

TH-070 and 2DG are known compounds that are not protected by patents as compounds per se.

TH-070 and 2DG are known compounds that are no longer eligible for patent protection as compounds per se. A compound per se patent excludes others from making, using or selling the patented compound, regardless of how or for what purpose the compound is formulated or intended to be used. Consequently, these compounds and certain of their uses are in the public domain. Acraf, S.p.a. has rights to market TH-070 in certain European countries for the treatment of certain cancer indications, and we cannot prevent its sale for these indications or for indications where we have not received patent protection. Even if we obtain patents for TH-070 to treat BPH, there may be off-label use of competitive products for our patented indications.

We have in-licensed one issued patent that covers the treatment of breast cancer with 2DG in combination with paclitaxel or docetaxel and related applications that cover other combination therapies, but there can be no assurance that any other patent application under this license will be issued. As a result, others may develop and market 2DG for the treatment of other cancers, or for the treatment of breast cancer in combination with chemotherapy agents where we do not obtain patents claiming such use.

Metabolic Targeting is not protected by patents, and others may be able to develop competitive drugs using this approach.

We do not have issued patents or patent applications that would prevent others from taking advantage of Metabolic Targeting generally to discover and develop new therapies for cancer, BPH or other diseases. Consequently, our competitors may seek to discover and develop potential therapeutics that operate by mechanisms of action that are the same or similar to the mechanisms of action of our product candidates.

We are dependent on patents and proprietary technology, both our own and those licensed from others. If we or our licensors fail to adequately protect this intellectual property or if we do not have exclusivity for the marketing of our products, our ability to commercialize products could suffer.

Our commercial success will depend in part on our ability and the ability of our licensors to obtain and maintain patent protection sufficient to prevent others from marketing our product candidates, as well as to successfully defend and enforce these patents against infringement and to operate without infringing the proprietary rights of others. We will only be able to protect our product candidates from unauthorized use by third parties to the extent that valid and enforceable patents cover our product candidates or they are effectively protected by trade secrets. If our patents, or those patents we have licensed are found to be invalid, we will lose the ability to exclude others from making, using or selling the inventions claimed therein. We have a limited number of patents and pending patent applications.

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The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the United States. The laws of many countries may not protect intellectual property rights to the same extent as United States laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights. 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. Accordingly, we do not know whether any of our patent applications will result in the issuance of any patents, and we cannot predict the breadth of claims that may be allowed in our patents or in the patents we license from others.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our or our licensors' pending patent applications and issued patents, and we may have to participate in expensive and protracted interference proceedings to determine priority of invention;
- we or our licensors might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative product candidates or duplicate any of our or our licensors' product candidates;
- our or our licensors' pending patent applications may not result in issued patents;
- our or our licensors' issued patents may not provide a basis for commercially viable products or may not provide us with any competitive advantages or may be challenged by third parties;
- others may design around our or our licensors' patent claims to produce competitive products which fall outside the scope of our or our licensors' patents;
- we may not develop or in-license additional patentable proprietary technologies related to our product candidates; or
- the patents of others may prevent us from marketing one or more of our product candidates for one or more indications that may be valuable to our business strategy.

Moreover, an issued patent does not guarantee us the right to practice the patented technology or commercialize the patented product. Third parties may have blocking patents that could be used to prevent us from commercializing our patented products and practicing our patented technology. Our issued patents and those that may be issued in the future may be challenged, invalidated or circumvented, which could limit our ability to prevent competitors from marketing related product candidates or could limit the length of the term of patent protection of our product candidates. In addition, the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. For these reasons, we may have competition for our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates 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 rely on trade secrets and other forms of non-patent intellectual property protection. If we are unable to protect our trade secrets, other companies may be able to compete more effectively against us.

We rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be made public during the regulatory approval

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process. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to or may not protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we are sued for infringing intellectual property rights of third parties or if we are forced to engage in an interference proceeding, it will be costly and time consuming, and an unfavorable outcome in that litigation or interference would have a material adverse effect on our business.

Our ability to commercialize our product candidates depends on our ability to develop, manufacture, market and sell our product candidates without infringing the proprietary rights of third parties. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the general field of cancer and BPH therapies or in fields that otherwise may relate to our product candidates. We are also aware of a patent that claims certain agents, including 2DG, to inhibit the import of glucose-6-phosphate into the endoplasmic reticulum of a cell. We do not know whether administration of 2DG for our intended uses inhibits such import. If it does, we would be required to license the patent or risk that a claim of infringement could be made. If we are shown to infringe, we could be enjoined from use or sale of the claimed invention if we are unable to prove that the patent is invalid. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our product candidates or any other compound that we may develop, may infringe, or which may trigger an interference proceeding regarding one of our owned or licensed patents or applications. There could also be existing patents of which we are not aware that our product candidates may inadvertently infringe or which may become involved in an interference proceeding.

The biotechnology and biopharmaceutical industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. For so long as our product candidates are in clinical trials, we believe our clinical activities fall within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the United States, which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. As our clinical investigational drugs progress toward commercialization, the possibility of a patent infringement claim against us increases. While we attempt to ensure that our active clinical investigational drugs and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties' patents and other proprietary rights. However, there can be no assurance they do not, and competitors or other parties may assert that we infringe their proprietary rights in any event.

We may be exposed to future litigation based on claims that our product candidates, or the methods we employ to manufacture them, infringe the intellectual property rights of others. Our ability to manufacture and commercialize our product candidates may depend on our ability to demonstrate that the manufacturing processes we employ and the use of our product candidates do not infringe third-party patents. If third-party patents were found to cover our product candidates or their use or manufacture, we could be required to pay damages or be enjoined and therefore unable to commercialize our product candidates, unless we obtained a license. A license may not be available to us on acceptable terms, if at all.

RISKS RELATED TO OUR INDUSTRY

If our competitors are able to develop and market products that are more effective, safer or more affordable than ours, or obtain marketing approval before we do, our commercial opportunities may be limited.

Competition in the biotechnology and pharmaceutical industries is intense and continues to increase, particularly in the area of cancer treatment. Most major pharmaceutical companies and many biotechnology companies are aggressively pursuing oncology development programs, including traditional therapies and

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therapies with novel mechanisms of action. Our cancer product candidates face competition from established biotechnology and pharmaceutical companies, including Aventis, Lilly, Pfizer and SuperGen and from generic pharmaceutical manufacturers. In particular, our glufosfamide product candidate for pancreatic cancer will compete with Gemzar, marketed by Lilly, and 5-fluorouracil, or 5-FU, a generic product which is sold by many manufacturers. In addition, Camptosar[®], marketed by Pfizer, and Taxotere, marketed by Aventis, are under investigation as possible combination therapies for first-line treatment of pancreatic cancer, and Tarceva is being evaluated as a single-agent therapy for the first-line treatment of pancreatic cancer by OSI Pharmaceuticals, Genentech and Roche. Orathecin[™] from SuperGen is under NDA review by the FDA for second-line treatment of pancreatic cancer as an oral agent, which may provide advantages to patients compared to glufosfamide, which is delivered intravenously. PANVAC[™]-VF, a vaccine under development by Therion Biologics, is also entering Phase 3 trials as a second-line treatment for pancreatic cancer.

Currently available BPH drugs are marketed by large pharmaceutical companies with significantly more experience and resources than we have. Our TH-070 product candidate for the treatment of symptomatic BPH will compete with alpha adrenergic receptor blockers, including Flomax[®], co-marketed by Boehringer Ingelheim and Abbott Laboratories, and Cardura[®], marketed by Pfizer, and with 5-alpha reductase inhibitors, including Proscar[®], marketed by Merck, Avodart[®], marketed by GlaxoSmithKline, and Xatral[®], marketed by the sanofi-aventis Group. In addition, we are aware that several other companies are developing drugs to treat BPH. We also will compete with other treatment alternatives such as surgery and other non-drug interventions.

We also face potential competition from academic institutions, government agencies and private and public research institutions engaged in the discovery and development of drugs and therapies. Many of our competitors have significantly greater financial resources and expertise in research and development, preclinical testing, conducting clinical trials, obtaining regulatory approvals, manufacturing, sales and marketing than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established pharmaceutical companies.

Our competitors may succeed in developing products that are more effective, have fewer side effects and are safer or more affordable than our product candidates, which would render our product candidates less competitive or noncompetitive. These competitors also compete with us to recruit and retain qualified scientific and management personnel, establish clinical trial sites and patient registration for clinical trials, as well as to acquire technologies and technology licenses complementary to our programs or advantageous to our business. Moreover, competitors that are able to achieve patent protection, obtain regulatory approvals and commence commercial sales of their products before we do, and competitors that have already done so, may enjoy a significant competitive advantage.

There is a substantial risk of product liability claims in our business. If we do not obtain sufficient liability insurance, a product liability claim could result in substantial liabilities.

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and marketing of human therapeutic products. Regardless of merit or eventual outcome, product liability claims may result in:

- delay or failure to complete our clinical trials;
- withdrawal of clinical trial participants;
- decreased demand for our product candidates;
- injury to our reputation;
- litigation costs;
- substantial monetary awards against us; and
- diversion of management or other resources from key aspects of our operations.

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If we succeed in marketing products, product liability claims could result in an FDA investigation of the safety or efficacy of our products, our manufacturing processes and facilities or our marketing programs. An FDA investigation could also potentially lead to a recall of our products or more serious enforcement actions, or limitations on the indications for which they may be used, or suspension or withdrawal of approval.

We have product liability insurance that covers our clinical trials up to a \$3 million annual aggregate limit. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for our product candidates or any other compound that we may develop. However, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or at all, and the insurance coverage that we obtain may not be adequate to cover potential claims or losses.

Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which would negatively affect our ability to achieve profitability.

Our product candidates may not gain market acceptance among physicians, patients, healthcare payors and the medical community. The degree of market acceptance of any approved products will depend on a number of factors, including:

- the effectiveness of the product;
- the prevalence and severity of any side effects;
- potential advantages or disadvantages over alternative treatments;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the price of the product, both in absolute terms and relative to alternative treatments; and
- sufficient third-party coverage or reimbursement.

If our product candidates receive regulatory approval but do not achieve an adequate level of acceptance by physicians, healthcare payors and patients, we may not generate product revenues sufficient to attain profitability.

If third-party payors do not adequately reimburse patients for any of our product candidates, if approved for marketing, we may not be successful in selling them.

Our ability to commercialize any products successfully will depend in part on the extent to which reimbursement will be available from governmental and other third-party payors, both in the United States and in foreign markets. Even if we succeed in bringing one or more products to the market, the amount reimbursed for our products may be insufficient to allow our products to compete effectively with products that are reimbursed at a higher level. If the price we are able to charge for any products we develop is inadequate in light of our development costs, our profitability could be adversely affected.

Reimbursement by a governmental and other third-party payor may depend upon a number of factors, including the governmental and other 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.

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Obtaining reimbursement approval for a product from each third-party and government 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 obtain reimbursement.

Eligibility for coverage does not imply that any drug product will be reimbursed in all cases or at a rate that allows us to make a profit. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not become permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or Medicare or Medicaid data used to calculate these rates. Net prices for products also may be reduced by mandatory discounts or rebates required by government health care programs or by any future relaxation of laws that restrict imports of certain medical products from countries where they may be sold at lower prices than in the United States.

The health care industry is experiencing a trend toward containing or reducing costs through various means, including lowering reimbursement rates, limiting therapeutic class coverage and negotiating reduced payment schedules with service providers for drug products. The Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA) became law in November 2003 and created a broader prescription drug benefit for Medicare beneficiaries. The MMA also contains provisions intended to reduce or eliminate delays in the introduction of generic drug competition at the end of patent or nonpatent market exclusivity. The impact of the MMA on drug prices and new drug utilization over the next several years is unknown. The MMA also made adjustments to the physician fee schedule and the measure by which prescription drugs are presently paid, changing from Average Wholesale Price to Average Sales Price. The effects of these changes are unknown but may include decreased utilization of new medicines in physician prescribing patterns, and further pressure on drug company sponsors to provide discount programs and reimbursement support programs. There have been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services, which may affect reimbursement levels for our future products. In addition, the Centers for Medicare and Medicaid Services frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates and may have sufficient market power to demand significant price reductions.

Foreign governments tend to impose strict price controls, which may adversely affect our future profitability.

In some foreign countries, particularly in the European Union, prescription drug pricing 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 profitability will be negatively affected.

We may incur significant costs complying with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.

Our research and development activities use biological and hazardous materials that are dangerous to human health and safety or the environment. We are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these materials and wastes resulting from these materials. We are also subject to regulation by the Occupational Safety and Health Administration, or OSHA, the California and federal environmental protection agencies and to regulation under the Toxic Substances Control Act. OSHA or the California or federal EPA may adopt regulations that may affect

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our research and development programs. We are unable to predict whether any agency will adopt any regulations that could have a material adverse effect on our operations. We have incurred, and will continue to incur, capital and operating expenditures and other costs in the ordinary course of our business in complying with these laws and regulations.

Although we believe our safety procedures for handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot entirely eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of hazardous materials. In the event of contamination or injury, we could be held liable for any resulting damages, and any liability could significantly exceed our insurance coverage.

We may not be able to conduct, or contract with others to conduct, animal testing in the future, which could harm our research and development activities.

Certain laws and regulations relating to drug development require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

RISKS RELATED TO OUR COMMON STOCK

The price of our common stock may be volatile and you may not be able to sell your shares at or above the initial offering price.

Prior to this offering, there has been no public market for our common stock. An active and liquid trading market for our common stock may not develop or be sustained following this offering. The market price for our common stock may decline below the initial public offering price and our stock price is likely to be volatile. You may not be able to sell your shares at or above the initial public offering price. The stock markets in general, and the markets for biotechnology stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock.

Price declines in our common stock could result from general market and economic conditions and a variety of other factors, including:

- adverse results or delays in our clinical trials of glufosfamide, TH-070 or 2DG;
- announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;
- adverse actions taken by regulatory agencies with respect to our product candidates, clinical trials, manufacturing processes or sales and marketing activities;
- announcements of technological innovations or new products by our competitors;
- regulatory developments in the United States and foreign countries;
- any lawsuit involving us or our product candidates;
- announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;
- developments concerning our strategic alliances or acquisitions;
- actual or anticipated variations in our operating results;

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- changes in recommendations by securities analysts or lack of analyst coverage;
- deviations in our operating results from the estimates of analysts;
- sales of our common stock by our executive officers, directors and five percent stockholders or sales of substantial amounts of common stock;
- changes in accounting principles; and
- loss of any of our key scientific or management personnel.

In the past, following periods of volatility in the market price of a particular company's securities, litigation has often been brought against that company. If litigation of this type is brought against us, it could be extremely expensive and divert management's attention and the company's resources.

We will have broad discretion in how we use the net proceeds from this offering, and we may not use them effectively.

Our management will have considerable discretion in the application of the net proceeds of the offering. We currently intend to use the net proceeds from this offering to fund expenses related to clinical trials, other research and development, sales and marketing and for general corporate purposes and for working capital. However, our plans may change and we could spend the net proceeds in ways that do not necessarily enhance the value of our common stock.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

If you purchase shares in this offering, the value of your shares based on our actual book value will immediately be less than the offering price you paid. This reduction in the value of your equity is known as dilution. This dilution occurs in large part because our earlier investors paid substantially less than the initial public offering price when they purchased their shares. Investors purchasing common stock in this offering will, therefore, incur immediate dilution of \$ _____ in net tangible book value per share of common stock, based on an assumed initial public offering price of \$ _____ per share (the midpoint of the estimated range on the cover of this prospectus). Investors will incur additional dilution upon the exercise of outstanding stock options and an outstanding warrant. In addition, if we raise funds by issuing additional securities, the newly issued shares will further dilute your percentage ownership of our company.

If our officers, directors and largest stockholders choose to act together, they may be able to control our management and operations, acting in their best interests and not necessarily those of other stockholders.

After this offering, our officers, directors and holders of 5% or more of our outstanding common stock will beneficially own approximately _____ % of our common stock (after giving effect to the conversion of all outstanding shares of our preferred stock, but assuming no exercise of the underwriters' over-allotment option and no exercise of outstanding options or warrants). As a result, these stockholders, acting together, will be able to significantly influence all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with the interests of other stockholders, and they may act in a manner that advances their best interests and not necessarily those of other stockholders.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. If there are substantial sales of our common stock, the price of our common stock could decline.

Sales of substantial amounts of our common stock in the public market after the offering could adversely affect the price of our common stock. After consummation of this offering, our current stockholders will be

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subject to a 180-day lock-up on the sale of their shares. After the lock-up expires, at least _____ shares of our common stock will become freely tradeable, _____ shares of common stock will be tradeable subject to Rule 144 and holders of _____ shares of our common stock will have rights to cause us to file a registration statement on their behalf and to include their shares in registration statements that we may file on behalf of other stockholders. By exercising their registration rights, and selling a large number of shares, these holders could cause the price of our common stock to decline.

Our certificate of incorporation, our bylaws and Delaware law contain provisions that could discourage another company from acquiring us and may prevent attempts by our stockholders to replace or remove our current management.

Provisions of Delaware law, our certificate of incorporation and bylaws may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. 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 or remove our board of directors. These provisions include:

- authorizing the issuance of “blank check” preferred stock without any need for action by stockholders;
- providing for a classified board of directors with staggered terms;
- requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;
- eliminating the ability of stockholders to call special meetings of stockholders;
- prohibiting stockholder action by written consent; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled “Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and “Business,” contains forward-looking statements. We may, in some cases, use words such as “project,” “believe,” “anticipate,” “plan,” “expect,” “estimate,” “intend,” “should,” “would,” “could,” “potentially,” “will,” or “may,” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements in this prospectus may include statements about:

- our ability to commence, and the timing of, clinical trials for our glufosfamide, TH-070 and 2DG development programs;
- the completion and success of any clinical trials that we commence;
- our receipt of regulatory approvals;
- our ability to maintain and establish intellectual property rights in our product candidates;
- whether any product candidates we commercialize are safer or more effective than other marketed products, treatments or therapies;
- our research and development activities, including development of our new product candidates, and projected expenditures;
- our ability to successfully complete preclinical and clinical testing for new product candidates we develop or license;
- our ability to have manufactured sufficient supplies of API and drug product for clinical testing and commercialization;
- our ability to obtain licenses to any necessary third party intellectual property;
- our ability to retain and hire necessary employees and appropriately staff our development programs;
- our use of the proceeds from this offering;
- our cash needs; and
- our financial performance.

There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include those that we discuss in this prospectus under the caption “Risk Factors.” You should read these factors and the other cautionary statements made in this prospectus as being applicable to all related forward-looking statements wherever they appear in this prospectus. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. The forward-looking statements contained in this prospectus are excluded from the safe-harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

USE OF PROCEEDS

We estimate that our net proceeds from the sale of _____ shares of common stock in this offering will be approximately \$ _____ million, assuming an initial public offering price of \$ _____ per share, the mid-point of the estimated price range shown on the cover of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us. If the underwriters exercise their over-allotment option, we estimate that we will receive additional net proceeds of approximately \$ _____ million. We expect to use the net proceeds to fund:

- approximately \$45.0 million for the clinical development of glufosfamide, TH-070 and 2DG, including trials for additional indications;
- approximately \$8.0 million for research and development of additional product candidates;
- approximately \$3.0–10.0 million for initial development of sales and marketing infrastructure, depending on our commercialization strategy for TH-070; and
- the remainder for working capital, capital expenditures and other general corporate purposes, including potential strategic acquisitions.

Our cash on hand may also be used to fund the above programs. We expect our net proceeds from this offering, together with our cash on hand, will be sufficient to advance our clinical development programs to complete our Phase 3 clinical trial of glufosfamide for second-line treatment of pancreatic cancer, and to advance our TH-070 and 2DG clinical programs and our clinical program for glufosfamide for the first-line treatment of pancreatic cancer into Phase 3 trials.

The amounts and timing of our actual expenditures will depend upon numerous factors, including the timing and success of preclinical testing, the timing and success of our ongoing clinical trials and any clinical trials we may commence in the future, the timing of regulatory submissions, our commercialization strategy for TH-070, status of our research and development programs, the amount of proceeds actually raised in this offering and the amount of cash generated by our operations, if any. We may also use a portion of the proceeds for the acquisition of, or investment in, companies, technologies, products or assets that complement our business. However, we have no present understandings, commitments or agreements to enter into any potential acquisitions or investments. Our management will have broad discretion to allocate the net proceeds from this offering.

Pending use of the net proceeds as described above, we intend to invest the net proceeds of the offering in United States government and short-term investment grade securities.

DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to fund the development and expansion of our business, and therefore we do not anticipate paying cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, restrictions contained in future financing instruments and other factors our board of directors deems relevant.

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CAPITALIZATION

The following table describes our cash, cash equivalents and short-term investments and our capitalization as of September 30, 2004:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all of our outstanding preferred stock into 33,848,484 shares of our common stock upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale of _____ shares of common stock by us in this offering at an assumed initial public offering price of \$ _____ per share (the midpoint of the estimated price range shown on the cover of this prospectus), after deducting underwriting discounts and commissions and estimated offering costs to be paid by us.

	Actual	Pro Forma	Pro Forma As Adjusted
	(In thousands, except share and per share data)		
Cash and cash equivalents	\$ 16,237	\$ 16,237	\$
Notes payable, less current portion	\$ 185	\$ 185	\$
Redeemable convertible preferred stock, \$0.001 par value per share; 33,886,484 shares authorized; and 33,848,484 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	49,839	—	
Stockholders' equity (deficit):			
Preferred stock, \$ _____ par value per share; no shares authorized, actual and pro forma, and _____ shares authorized, pro forma as adjusted; and no shares outstanding, actual, pro forma or pro forma as adjusted			
Common stock, \$0.001 par value per share; 50,000,000 shares authorized, actual, pro forma, and pro forma as adjusted; and 5,548,047 shares issued and outstanding, actual; 39,396,531 shares issued and outstanding, pro forma; and _____ shares issued and outstanding pro forma as adjusted	6	39	
Additional paid-in capital	21,900	71,706	
Deferred stock-based compensation	(16,244)	(16,244)	
Accumulated other comprehensive income	98	98	
Deficit accumulated during the development stage	(26,700)	(26,700)	
Total stockholders' equity (deficit)	(20,940)	28,899	
Total capitalization	\$ 29,084	\$ 29,084	\$

The table above excludes:

- 437,000 shares of our common stock that were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 423,231 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2004 at a weighted average exercise price of \$0.24 per share;
- 38,000 shares of common stock issuable upon exercise of a warrant outstanding as of September 30, 2004 with an exercise price of \$1.00 per share, which does not expire upon the closing of this offering;
- 879,222 shares of common stock available for future grants under our 2001 Stock Option Plan as of September 30, 2004;
- 4,000,000 shares of common stock reserved for issuance under our 2004 Equity Incentive Plan; and
- _____ shares of common stock reserved for issuance under our 2004 Employee Stock Purchase Plan.

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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.

Our historical net tangible book value as of September 30, 2004 was approximately \$(20.9) million or \$(3.77) per share of common stock. Pro forma net tangible book value as of September 30, 2004 was approximately \$28.9 million or \$0.73 per share of common stock. Pro forma net tangible book value gives effect to the conversion of all of our outstanding redeemable convertible preferred stock into 33,848,484 shares of our common stock, which will occur automatically upon the closing of this offering.

After giving effect to the issuance and sale by us of the _____ shares of common stock offered by this prospectus, assuming an initial public offering price of \$ _____ per share (the midpoint of the estimated price range shown on the cover of this prospectus), after deducting underwriting discounts and commissions and estimated offering costs payable by us, our pro forma as adjusted net tangible book value as of _____, 2004 would have been approximately \$ _____ million, or \$ _____ per share. This represents an immediate increase in the pro forma net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution of \$ _____ per share to new investors. This dilution is illustrated by the following table:

Assumed initial public offering price per share	\$ _____
Historical net tangible book value per share as of September 30, 2004	(3.77)
Increase per share due to assumed conversion of all shares of convertible preferred stock	3.49

Pro forma net tangible book value per share before this offering	\$ 0.73
Increase per share attributable to this offering	_____

Pro forma as adjusted net tangible book value per share after the offering	_____

Dilution per share to new investors	\$ _____

The following table summarizes, as of September 30, 2004, the number of shares of common stock purchased from us, on a pro forma as adjusted basis to give effect to the conversion of all of our outstanding preferred stock into _____ shares of common stock, which will occur automatically upon the closing of this offering, and the total consideration and the average price per share paid by existing stockholders and new investors at an assumed initial public offering price of \$ _____ per share before deducting underwriting discounts and commissions and estimated offering costs payable by us:

	Total Shares		Total Consideration		Average Price Per Share
	Number	%	Amount	%	
Existing stockholders	39,396,531		\$ 50,712,000		\$ 1.29
New investors					
Totals					

The foregoing discussion and tables exclude:

- 437,000 shares of our common stock that were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 423,231 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2004 at a weighted average exercise price of \$0.24 per share;
- 38,000 shares of common stock issuable upon exercise of a warrant outstanding as of September 30, 2004 with an exercise price of \$1.00 per share, which does not expire upon the closing of this offering;

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- 879,222 shares of common stock available for future grants under our 2001 Stock Option Plan as of September 30, 2004;
- 4,000,000 shares of common stock reserved for issuance under our 2004 Equity Incentive Plan; and
- _____ shares of common stock reserved for issuance under our 2004 Employee Stock Purchase Plan.

In addition, we may grant more options or warrants in the future.

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

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

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SELECTED FINANCIAL DATA

We are a development stage company. The following selected statement of operations data for the period from October 17, 2001 (inception) to December 31, 2001 and the years ended December 31, 2002 and 2003, and balance sheet data as of December 31, 2002 and 2003, have been derived from our audited financial statements included elsewhere in this prospectus. The statements of operations data for the nine months ended September 30, 2003 and 2004 and the balance sheet data as of September 30, 2004, are derived from our unaudited financial statements appearing elsewhere in this prospectus, and in the opinion of management, include all adjustments, consisting of only normal recurring adjustments, necessary for a fair statement of the results for the unaudited interim period. The balance sheet data as of December 31, 2001, is derived from our financial data that are not included in this prospectus. The selected financial data set forth below should be read together with the financial statements and the related notes to those financial statements, as well as "Management's Discussion and Analysis of Financial Condition and Results of Operations," appearing elsewhere in this prospectus.

	Period from October 17, 2001 (date of inception) to December 31, 2001	Years Ended December 31,		Nine Months Ended September 30,		Cumulative Period from October 17, 2001 (date of inception) to September 30, 2004
		2002	2003	2003	2004	
(In thousands, except per share data)						
Operating expenses:						
Research and development	\$ 35	\$ 2,179	\$ 6,252	\$ 4,868	\$ 10,852	\$ 19,318
General and administrative	201	306	2,057	1,591	5,137	7,701
Total operating expenses	236	2,485	8,309	6,459	15,989	27,019
Loss from operations	(236)	(2,485)	(8,309)	(6,459)	(15,989)	(27,019)
Interest income	—	27	65	17	313	405
Interest expense	—	—	(59)	(24)	(27)	(86)
Net loss	(236)	(2,458)	(8,303)	(6,466)	(15,703)	(26,700)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	(40,862)	—	—	(40,862)
Net loss attributable to common stockholders	\$ (236)	\$ (2,458)	\$ (49,165)	\$ (6,466)	\$ (15,703)	\$ (67,562)
Net loss per common share:						
Basic and diluted	\$ (1.29)	\$ (21.19)	\$ (305.37)	\$ (40.92)	\$ (16.14)	
Weighted average number of shares used in per common share calculations:						
Basic and diluted	183	116	161	158	973	
Pro forma net loss per common share (unaudited) (see Note 13):						
Basic and diluted			\$ (4.04)		\$ (0.45)	
Weighted average number of shares used in pro forma per common share calculations (unaudited) (see Note 13):						
Basic and diluted			12,156		34,821	
As of December 31,						
	2001	2002	2003		As of September 30, 2004	
(In thousands)						
Balance Sheet Data:						
Cash and cash equivalents		\$ 187	\$ 6,215	\$ 40,609	\$ 16,237	
Working capital		2	6,154	40,177	28,587	
Total assets		195	6,726	41,270	31,375	
Notes payable, less current portion		—	—	242	185	
Redeemable convertible preferred stock		236	8,977	49,839	49,839	
Total stockholders' deficit		(107)	(2,667)	(9,695)	(20,940)	

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

The following discussion and analysis should be read in conjunction with our financial statements and related notes included elsewhere in this prospectus. This discussion may contain forward-looking statements based upon current expectations that involve risks and uncertainties, including those set forth under the heading "Risk Factors" and elsewhere in this prospectus. Our actual results and the timing of selected events discussed below could differ materially from those expressed in, or implied by, these forward-looking statements.

Overview

We are a biotechnology company focused on the discovery, development and commercialization of drugs based on Metabolic Targeting, an approach that targets fundamental differences in metabolism between normal and certain diseased cells. We are building a pipeline of drugs that are designed to selectively target tumor cells so that the drugs are less toxic to healthy tissues than conventional drugs, thereby providing improvements over current therapies.

Our initial clinical focus is the treatment of cancer and BPH. We have three product candidates. Glufosfamide, our lead product candidate for cancer, has completed two Phase 1 and five Phase 2 clinical trials in patients with various solid tumors. In September 2004, we initiated a pivotal Phase 3 clinical trial of glufosfamide for the second-line treatment of pancreatic cancer. We have received a special protocol assessment from the FDA for this trial. In addition, glufosfamide for the treatment of pancreatic cancer has received FDA fast track designation. TH-070, our lead product candidate for the treatment of symptomatic BPH, has completed enrollment in a Phase 2 clinical trial, which was commenced in the first quarter of 2004, and we are evaluating interim data. We plan to initiate a registrational program for TH-070 to treat symptomatic BPH in the first half of 2005. Our third product candidate, 2-deoxyglucose, or 2DG, our product candidate for the treatment of solid tumors, is being evaluated in a Phase 1 clinical trial as a combination therapy, which means that it is administered in conjunction with other chemotherapy treatments. This trial began in the first quarter of 2004. We are also working to discover novel drug candidates that are activated under the metabolic conditions typical of cancer cells, and we have identified lead compounds with promising *in vitro* data. In addition, we are investigating additional compounds for activity against BPH.

We are a development stage company and were incorporated in October 2001. We have devoted substantially all of our resources to research and development of our product candidates. We have not achieved any revenue from operations, and we have funded our operations through the private placement of equity securities. We have incurred a net loss from operations for the year ended December 31, 2003 of \$8.3 million and cumulative losses since our inception through September 30, 2004 of \$26.7 million. We expect our net losses to increase primarily due to our anticipated clinical trial activities. Clinical trials are costly, and as we continue to advance our product candidates through development, we expect our research and development expenses to increase significantly, especially as we continue our pivotal Phase 3 clinical trial of glufosfamide and begin a registrational program for TH-070 for the treatment of symptomatic BPH in the first half of 2005. Compared to Phase 1 and Phase 2 clinical trials, Phase 3 clinical trials typically involve a greater number of patients, may be conducted at multiple sites and in several countries, are conducted over a longer period of time and require greater quantities of drug product. Additionally we plan to significantly expand our infrastructure and facilities and hire additional personnel, including clinical development, research, administrative, sales and marketing personnel. We are unable to predict when, if ever, we will be able to commence sales of any product.

Revenues

We have not generated any revenues since our inception and do not expect to generate any revenues from the sale of our product candidates for many years.

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Research and Development Expenses

Research and development expenses consist primarily of costs of conducting clinical trials, salaries and related costs for personnel, costs for research projects and preclinical studies, costs related to regulatory filings, costs of clinical materials and facility costs. Consulting expenses are a significant component of our research and development expenses as we rely on expert consultants in many of the areas mentioned above. We recognize expenses as they are incurred. Our accruals for expenses associated with preclinical and clinical studies are based upon the terms of the service contracts, the amount of services provided and the status of the activities. We expect that research and development expenses will increase significantly in the future as we progress our product candidates through the more expensive later stage clinical trials, start additional clinical trials, progress our discovery research projects into the preclinical stage, file for regulatory approvals and hire more employees. From inception through September 30, 2004, we spent an aggregate of \$19.3 million on research and development expenses.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for our personnel in the executive, finance, patent, accounting and other administrative functions, as well as consulting costs for functions for which we either do not staff or only partially staff, including public relations, market research, business development, technical writing and accounting. Other costs include professional fees for legal and accounting services, insurance and facility costs. We anticipate that general and administrative expenses will increase significantly in the future as we continue to expand our operating activities and as a result of costs associated with being a public company. From inception through September 30, 2004, we spent an aggregate of \$7.7 million on general and administrative expenses.

Stock-Based Compensation

We use the intrinsic method of Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" ("APB No. 25"), in accounting for employee stock options, and present disclosure of pro forma information required under SFAS No. 123, "Accounting for Stock-Based Compensation" ("SFAS No. 123"), as amended by SFAS No. 148, "Accounting for Stock-Based Compensation—Transition and Disclosure—an amendment of FASB Statement No. 123" ("SFAS No. 148"). For stock options granted to employees no compensation expense is recognized unless the exercise price is less than fair market value at the date of grant. In anticipation of this offering, we have determined that, for accounting purposes, the estimated fair market value of our common stock was greater than the exercise price for certain options. As a result we have recorded deferred stock-based compensation for these options of \$18.1 million for the nine months ended September 30, 2004, \$2.3 million for the year ended December 31, 2003 and \$25,000 for the year ended December 31, 2002. This expense, which is a non-cash charge, will be amortized over the period in which the options vest, which is generally four years. The amortization of this expense recognized for the year ended December 31, 2003 was \$0.8 million, \$1,000 for the year ended December 31, 2002 and \$3.4 million for the nine months ended September 30, 2004. We expect the remaining \$16.2 million to be amortized as follows: \$1.8 million for the remaining three months of the year ending December 31, 2004, \$5.9 million for the year ending December 31, 2005, \$4.3 million for the year ending December 31, 2006, \$3.4 million for the year ending December 31, 2007, and \$0.8 million for the year ending December 31, 2008. During May 2004, the Company granted options to purchase 637,000 shares of common stock to employees, which require variable accounting. The measurement of stock-based compensation for these options is subject to periodic adjustment resulting from changes in the fair value of our common stock.

We account for equity instruments issued to non-employees in accordance with the provisions of SFAS No. 123 and Emerging Issues Task Force Issue No. 96-18, "Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services," which require that these equity instruments are recorded at their fair value on the measurement date. The measurement of stock-based compensation is subject to periodic adjustment as the underlying equity instruments vest. As a result, the non-cash

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charge to operations for non-employee options with vesting criteria is affected each reporting period by changes in the fair value of our common stock. For options granted to non-employees, we recorded \$0.3 million and \$21,000 of stock-based compensation expense during the years ended December 31, 2003 and 2002, respectively. We recorded \$0.4 million of stock-based compensation expense for the nine months ended September 30, 2004.

Results of Operations for the Nine Months Ended September 30, 2003 and 2004

Research and development expenses for the nine months ended September 30, 2004 were \$10.9 million compared to \$4.9 million for the nine months ended September 30, 2003. The \$6.0 million increase in research and development expenses was due primarily to a \$1.9 million increase in clinical trial costs, \$1.5 million increase in staffing and the associated expenses of salaries, benefits and other employee related costs, \$1.0 million increase in consulting and licensing costs and a \$1.4 million increase in stock-based compensation.

Research and development expenses associated with glufosfamide were \$4.7 million for the nine months ended September 30, 2004 and were \$8,000 for the nine months ended September 30, 2003. This increase was due to the activities leading up to and initiation of a Phase 3 clinical trial for the second time treatment of pancreatic cancer in 2004. Research and development expenses associated with TH-070 were \$2.2 million for the nine months ended September 30, 2004 and were \$0.2 million for the nine months ended September 30, 2003 because we did not commence this program until the second quarter of 2003. Research and development expenses associated with 2DG were \$2.0 million for the nine months ended September 30, 2004 and were \$4.2 million for the nine months ended September 30, 2003. This decrease resulted from the completion of a major portion of preclinical studies during 2003. Discovery research expenses were approximately \$2.0 million for the nine months ended September 30, 2004 and were \$0.5 million for the nine months ended September 30, 2003. We cannot predict when any net cash inflows from any of our product candidates will commence.

General and administrative expenses for the nine months ended September 30, 2004 were \$5.1 million versus \$1.6 million for the nine months ended September 30, 2003. The \$3.5 million increase in general and administrative expenses was due primarily to \$1.0 million attributable to increased staffing, \$1.3 million from stock-based compensation, \$0.6 million from increased spending on patent, legal, and audit services, and \$0.4 from other services, primarily public relations.

Interest income for the nine months ended September 30, 2004 was \$312,794 compared to \$17,488 for the nine months ended September 30, 2003. The increase in interest income was the result of interest earned on the \$40.9 million of net proceeds from the sale of Series B convertible preferred stock in November 2003.

Interest expense for the nine months ended September 30, 2004 was \$27,057 compared to \$24,429 for the nine months ended September 30, 2003. The increase in interest expense was the result of interest incurred under the Company's 2003 line of credit and amortization of debt issuance costs associated with warrants issued in connection with the line of credit.

Results of Operations

Years ended December 31, 2003 and 2002 and the period from October 17, 2001 (date of inception) to December 31, 2001

We have a limited operating history. Presented below is a comparison of our results of operations for the year ended December 31, 2003 compared to the year ended December 31, 2002 and the period from October 17, 2001 (date of inception) to December 31, 2001. Our first full year of operations was 2002.

Research and Development

Research and development expenses for the year ended December 31, 2003 were \$6.3 million compared to \$2.2 million for the year ended December 31, 2002. The increase in research and development expenses was primarily due to increases of \$1.3 million associated with increased staffing levels, \$0.9 million for preclinical

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studies, \$0.7 million for supplies and facilities, \$0.4 million for manufacturing and testing of clinical material drug supply and \$0.3 million for consulting and scientific advisory costs. Non-cash stock-based compensation expenses associated with option issuances to our research and development staff and consultants were \$0.3 million in 2003 and \$21,000 in 2002.

Research and development expenses for the year ended December 31, 2002 were \$2.2 million compared to \$35,000 for the period from October 17, 2001 (date of inception) to December 31, 2001. This increase was primarily due to increases of \$1.4 million associated with increased staffing and consulting costs, \$0.3 million for facilities costs, \$0.2 million for preclinical studies and as a result of conducting operations for a full year. Research and development expenses for the period from October 17, 2001 (date of inception) to December 31, 2001 were primarily comprised of supplies and facilities costs.

Research and development expenses associated with glufosfamide for 2003 were not significant because this product candidate was in-licensed in the third quarter of 2003. Research and development expenses associated with TH-070 in 2003 were \$0.4 million. Research and development expenses associated with 2DG for 2003 were \$4.2 million and discovery research expenses were approximately \$1.7 million in 2003. We did not track research and development cost information by program prior to 2003.

General and Administrative

General and administrative expenses were \$2.1 million for the year ended December 31, 2003 compared to \$0.3 million for the year ended December 31, 2002. The increase in general and administration expenses was primarily due to costs of \$0.5 million associated with increases in staffing levels including adding a Chief Executive Officer, a Chief Financial Officer and a Vice President of Intellectual Property. Consulting costs increased by \$0.2 million for market research, financial and business development support. Non-cash stock-based compensation expenses associated with option issuances to our administrative personnel were \$0.8 million in 2003 and \$1,000 in 2002.

General and administrative expenses for the year ended December 31, 2002 were \$0.3 million compared to \$0.2 million for the period ended December 31, 2001. This increase was primarily due to increased legal expenses.

General and administrative expenses for the period from October 17, 2001 (date of inception) to December 31, 2001 were \$0.2 million, which consisted primarily of salary and expenses for the company's sole employee and founder and costs associated with establishing operations.

Interest Income (Expense)

Interest income for the year ended December 31, 2003 was \$65,000 compared to \$27,000 for the year ended December 31, 2002. The increase in interest income was principally attributable to the interest earned on the \$40.9 million of net proceeds from the sale of our Series B convertible preferred stock in November 2003. There was no interest income for the period from October 17, 2001 (date of inception) to December 31, 2001.

Interest expense was \$59,000 for the year ended December 31, 2003 which consists of interest incurred under our March 2003 line of credit and amortization of debt issuance costs associated with warrants issued in connection with the line of credit. There was no interest expense for the year ended December 31, 2002 or for the period from October 17, 2001 (date of inception) to December 31, 2001.

We incurred net operating losses for the years ended December 31, 2002 and 2003 and the period ended December 31, 2001 and, accordingly, we did not pay any federal or state income taxes. As of December 31, 2003, we had accumulated approximately \$8.6 million and \$8.3 million in federal and state net operating loss carryforwards, respectively, to reduce future taxable income. If not utilized, our federal and state net operating loss carryforwards will begin to expire in various amounts in 2021 and 2011, respectively. Our net operating loss

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carryforwards are subject to certain limitations on annual utilization in case of changes in ownership, as defined by federal and state tax laws.

Income Taxes

We have not recorded a benefit from our net operating loss carryforwards because we believe that it is uncertain that we will have sufficient income from future operations to realize the carryforwards prior to their expiration. Accordingly, we have established a valuation allowance against the deferred tax asset arising from the carryforwards.

At December 31, 2003, we had research credit carryforwards of approximately \$0.2 million and \$0.2 million for federal and California state income tax purposes, respectively. If not utilized, the federal carryforwards will expire in various amounts beginning in 2011. The California state research credit can be carried forward indefinitely.

Beneficial Conversion Feature

In November 2003, we sold 24,848,484 shares of Series B redeemable convertible preferred stock for aggregate net proceeds of approximately \$40.9 million. The issuance of the Series B redeemable convertible preferred stock resulted in a beneficial conversion feature, calculated in accordance with EITF 00-27, "Application of Issue No. 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features of Contingently Adjustable Conversion Ratios*" to *Certain Convertible Instruments*" based upon the conversion price of the preferred stock into shares of common stock, and the fair market value of the common stock at the date of issue. Accordingly, for the year ended December 31, 2003, we recognized approximately \$40.9 million as a charge to additional paid-in-capital to account for the deemed dividend on the redeemable convertible preferred stock as of the issuance date. In accordance with the provisions of EITF 00-27, the amount of the deemed dividend related to the beneficial conversion feature is limited to the net proceeds received for the sale of the securities.

Liquidity and Capital Resources

We have incurred net losses since inception through September 30, 2004, of \$26.7 million. We have not generated any revenues and do not expect to generate revenue from product candidates for several years. Since inception, we have funded our operations primarily through the private placement of our preferred stock. We raised \$9.0 million through the sale of our Series A convertible preferred stock in 2001 and 2002 and \$40.9 million through the sale of our Series B convertible preferred stock in November 2003.

At September 30, 2004, we had cash and cash equivalents of \$16.2 million compared to \$40.6 million at December 31, 2003. Net cash used in operating activities for the nine months ended September 30, 2004 and 2003 was \$12.0 million and \$5.1 million, respectively. For the nine months ended September 30, 2004 cash used in operations was attributable primarily to our net loss after adjustments for non-cash charges related to the amortization of deferred stock-based compensation and an increase in accounts payable resulting primarily from increased research and development activities and an increase in prepaid expenses related to our proposed initial public offering. For the nine months ended September 30, 2003 cash used in operations was attributable primarily to our net loss and a decrease in accounts payable partially offset by an increase in accrued liabilities and a decrease in prepaids and other current assets. Net cash used in investing activities was \$13.2 million and \$0.2 million for the nine months ended September 30, 2004 and 2003, respectively, primarily for marketable securities in 2004 and the acquisition of property and equipment in 2003. Net cash generated by financing activities was primarily generated by the exercise of employee stock options in 2004 and the issuance of an equipment financing note in 2003.

Net cash used in operating activities for the periods ended December 31, 2003, 2002 and 2001 was \$6.7 million, \$2.5 million and \$0.1 million, respectively. For the year ended December 31, 2003, cash used in

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operations was attributable primarily to our net losses after adjustments for non-cash charges related to amortization of deferred stock-based compensation, an increase in accrued liabilities resulting primarily from increased research and development activities and depreciation. For the year ended December 31, 2002, cash used in operations was attributable primarily to our net losses after adjustments for non-cash charges related to increase in accounts payable and depreciation. The use of cash in the period ended December 31, 2001 was attributable to our net loss partially offset by increases in accounts payable and accrued liabilities.

Net cash used in investing activities was \$0.2 million for the year ended December 31, 2003 for the purchase of equipment. For the year ended December 31, 2002, net cash used in investing activities was \$0.2 million for the purchase of two certificates of deposit that serve as collateral for our facility lease and for a line of credit agreement, and the purchase of equipment and marketable securities.

Net cash provided by financing activities for the years ended December 31, 2003 and 2002, and the period from October 17, 2001 (date of inception) to December 31, 2001 was \$41.3 million, \$8.7 million and \$0.2 million, respectively. The net cash provided by financing activities was primarily attributable to the sale of redeemable convertible preferred stock. Cash provided for the year ended December 31, 2003 also included \$0.4 million of net proceeds under the line of credit.

In November 2004, we entered into a Development Agreement with MediBIC Co., Ltd. Under this agreement, in December 2004 we received an upfront payment of \$4.75 million to support the development of glufosfamide in the Asian countries covered by the agreement and an option payment of \$250,000. We will be required to refund these payments and the agreement will terminate if we and MediBIC cannot agree to a development plan for glufosfamide for the treatment of certain cancers in Asian countries covered by the agreement by March 1, 2005, or a later date agreed by the parties. We are responsible for all development activities, and MediBIC has no other funding obligations. We have agreed to pay MediBIC a percentage of net sales or net revenues from the sale of glufosfamide products for the treatment of cancer by us or third parties in the Asian countries covered by the agreement. We may also be required to pay MediBIC a percentage of upfront or milestone payments we receive from any third-party sublicensee of ours for the development of a glufosfamide product for the treatment of cancer in those Asian countries. We cannot be certain when, if ever, we will have to make these royalty, upfront or milestone payments. We may terminate the agreement at any time by making certain payments to MediBIC ranging from \$5.25 to \$15 million, depending on the stage of development.

Developing drugs, conducting clinical trials, and commercializing products is expensive. Our future funding requirements will depend on many factors, including:

- the progress and costs of our clinical trials and other research and development activities;
- the costs and timing of obtaining regulatory approval;
- the costs of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights;
- the costs and timing of securing manufacturing capabilities for our clinical product candidates and commercial products, if any;
- the costs of establishing sales, marketing and distribution capabilities; and
- the terms and timing of any collaborative, licensing and other arrangements that we may establish.

We expect to incur losses from operations in the future. We expect to incur increasing research and development expenses, including expenses related to clinical trials and additional personnel. We expect that our general and administrative expenses will increase in the future as we expand our staff, add infrastructure and incur additional expenses related to being a public company, including directors' and officers' insurance, investor relations and increased professional fees.

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We believe that the net proceeds from this offering, together with our cash on hand, will be sufficient to fund our projected operating requirements for at least the next two years including our planned clinical trials of glufosfamide, TH-070 and 2DG, the research and development of additional product candidates, the initial development of a sales and marketing effort, working capital and general corporate purposes. However, we may need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic, market conditions and other factors, many of which are beyond our control. There can be no assurance that sufficient funds will be available to us when required or on satisfactory terms. If necessary funds are not available, we may have to delay, reduce the scope or eliminate some of our research and development, which could delay the time to market for any of our product candidates. We may also need to seek funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Obligations and Commitments

In March 2003, we entered into a loan and security agreement with Silicon Valley Bank to borrow up to \$1.0 million for working capital and equipment purchases. Through September 30, 2004, we have borrowed approximately \$0.6 million under this facility, which will be repaid over a 36-month period from the date of borrowing. These borrowings bear interest at the rate of 5.7% per year at September 30, 2004. In addition we issued a warrant to Silicon Valley Bank to purchase up to 38,000 shares of Series A convertible preferred stock in connection with the loan agreement. We may borrow the remaining \$0.4 million available under this facility, as amended, until March 31, 2005. At September 30, 2004 the amount due under this facility was \$0.4 million. The financial covenant in this agreement requires us to maintain the lower of 85% of our total cash and cash equivalents or \$10.0 million at Silicon Valley Bank. At September 30, 2004 we were in compliance with our covenant.

We have a sublease for facilities that expires on February 28, 2010 and another sublease for facilities that expires on December 31, 2004.

As of September 30, 2004, future minimum payments under our subleases and financing line are as follows (in thousands):

	<u>Within one year</u>	<u>One to three years</u>	<u>Four to five years</u>	<u>After five years</u>	<u>Total</u>
Facilities subleases	\$ 481	\$ 1,302	\$ 752	\$ —	\$2,535
Financing line	186	211	—	—	397
Total	\$ 667	\$ 1,513	\$ 752	\$ —	\$2,932

In August 2003, we entered into an agreement with Baxter International, Inc. and Baxter Healthcare S.A. for the licensing and development of glufosfamide. Under this agreement, we paid Baxter an upfront license fee of \$100,000 and a \$100,000 development milestone in 2003. We also made a development milestone payment of \$1.3 million in November 2004 and we are obligated to make certain additional development milestone payments, with the next payment due in connection with the filing of a new drug application with the FDA for glufosfamide. Future milestone payments in connection with the development of glufosfamide and United States and foreign regulatory submissions could total up to \$8.0 million, and sales-based milestone payments could total up to \$17.5 million. Following regulatory approval, we will be obligated to pay royalties to Baxter based on sales of glufosfamide products. We cannot be certain when, if ever, we will have to make development- or sales-based milestone or royalty payments to Baxter.

Under our license agreement with Dr. Theodore J. Lampidis and Dr. Waldemar Priebe for rights under a patent and certain patent applications that generally cover the treatment of cancer with 2DG in combination with certain other cancer drugs, we are obligated to make certain milestone payments, including milestone payments

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of up to \$700,000 in connection with the filing and approval of an NDA for the first product covered by the licensed patents, as well as royalties based on sales of such products. We cannot be certain when, if ever, we will have to make these milestone or royalty payments.

In June 2004, we entered into an agreement with Acraf, S.p.a. for rights to use Acraf's regulatory documents and pre-clinical and clinical information pertaining to the active ingredient in TH-070 for our regulatory filings on TH-070-based products and for obtaining marketing authorizations world-wide for such products. In consideration for our licenses under this agreement, we paid Acraf a one-time payment of €300,000, or approximately \$374,000, in 2004. We are also obligated to pay Acraf milestone payments, with the next such milestone payment due in connection with the marketing approval of our first TH-070-based product in certain specified territories. In addition, there is a sales-based milestone due should sales of a Threshold product containing TH-070 exceed €50 million in one year. Future aggregate milestone payments under this agreement could total €1.8 million.

Off-Balance Sheet Liabilities

As of December 31, 2001, 2002, 2003 and September 30, 2004, we did not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. In addition, we do not engage in trading activities involving non-exchange traded contracts. Therefore, we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these relationships.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and related disclosures. We review our estimates on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our financial statements included in this prospectus, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Stock-Based Compensation

We account for stock-based employee compensation arrangements in accordance with the provisions of APB No. 25 and SFAS No. 123 and comply with the disclosure requirements of SFAS No. 148. Under APB No. 25, compensation expense is based on the difference, if any, on the date of grant, between the estimated fair value of our common stock and the exercise price. SFAS No. 123 defines a "fair value" based method of accounting for an employee stock option or similar equity investment.

The fair value of the common stock for options granted through September 30, 2004, was originally estimated by our board of directors, with input from management. We did not obtain contemporaneous valuations by an unrelated valuation specialist. Subsequently, we reassessed the valuations of common stock relating to grants of options during the years ended December 31, 2002 and 2003 and for the nine months ended September 30, 2004. As disclosed more fully in Note 9 of the notes of our financial statements, we granted stock options and restricted common stock with exercise prices ranging from \$0.10 to \$0.32 during the years ended December 31, 2002 and 2003 and for the nine months ended September 30, 2004. In addition, we determined that the fair value of our common stock increased from \$0.10 to \$9.95 per share during that period.

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For financial reporting purposes, we have recorded stock-based compensation representing the difference between the estimated fair value of common stock and the option exercise price. Because shares of our common stock have not been publicly traded, we determined the estimated fair value based upon several factors, including significant milestones attained, sales of our redeemable convertible preferred stock, changes in valuations of existing comparable publicly-registered biotech companies, trends in the broad market for biotechnology stocks and the expected valuation we would obtain in an initial public offering. Although it is reasonable to expect that the completion of our initial public offering will add value to the shares as a result of increased liquidity and marketability, the amount of additional value cannot be measured with precision or certainty. We amortize employee stock-based compensation on a straight-line basis for equity instruments subject to fixed accounting. We amortize employee stock-based compensation in accordance with the provisions of FASB Interpretation No. 28, *“Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans”* for equity instruments subject to variable accounting.

We account for equity instruments issued to non-employees in accordance with the provisions of SFAS No. 123 and Emerging Issues Task Force (“EITF”) Issue No. 96-18, *“Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods, or Services.”*

As a result, the non-cash charge to operations for non-employee options with vesting or other performance criteria is affected each reporting period by changes in the estimated fair value of our common stock. The two factors which most affect these changes are the fair value of the common stock underlying stock options for which stock-based compensation is recorded and the volatility of such fair value. If our estimates of the fair value of these equity instruments change, it would have the effect of changing compensation expenses.

Preclinical and Clinical Trial Accruals

We record accruals for estimated preclinical and clinical trial costs. These costs have been a significant component of research and development expenses. We accrue for the costs of preclinical and clinical trials based upon estimates of work completed under service agreements. These estimates include the assessment of information received from third-party organizations and the overall status of preclinical and clinical trial activities, however, our estimates may not match the timing of actual services performed by the organizations, which may result in adjustments to our research and development expenses in future periods. To date we have had no such adjustments.

Accounting for Income Taxes

Our income tax policy records the estimated future tax effects of temporary differences between the tax basis of assets and liabilities and amounts reported in the accompanying balance sheets, as well as operating loss and tax credit carry forwards. We have recorded a full valuation allowance to reduce our deferred tax asset, as based on available objective evidence; it is more likely than not that the deferred tax asset will not be realized. In the event that we were to determine that we would be able to realize our deferred tax assets in the future, an adjustment to the deferred tax asset would increase net income in the period such determination was made.

Recent Accounting Pronouncements

In May 2003, the FASB issued SFAS No. 150, *“Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity”* (“SFAS No. 150”). SFAS No. 150 establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equities. It requires that an issuer classify a financial instrument that is within its scope as a liability or an asset in some circumstances. Many of those instruments were previously classified as equity. SFAS No. 150 is effective for financial instruments entered into or modified after May 31, 2003, and otherwise is effective at the beginning of the first interim period beginning after June 15, 2003. In November 2003, certain elements of SFAS No. 150 were deferred to fiscal periods beginning after December 15, 2004. SFAS No. 150 is to be implemented by reporting the cumulative effect of a change in an accounting principle for financial instruments created before the

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issuance date of SFAS No. 150 and still existing at the beginning of the interim period of adoption. Restatement is not permitted. The adoption of the effective elements of SFAS No. 150 had no material effect on our financial position or results of operations. We do not expect the adoption of the deferred elements of SFAS No. 150 to have a material impact on our financial position or our results of our operations.

In December 2003, the FASB issued a revised FASB Interpretation No. 46 ("FIN No. 46R"), "*Consolidation of Variable Interest Entities, an interpretation of ARB No. 51.*" The FASB published the revision to clarify and amend some of the original provisions of FIN No. 46, which was issued in January 2003, and to exempt certain entities from its requirements. A variable interest entity ("VIE") refers to an entity subject to consolidation according to the provisions of this Interpretation. FIN No. 46R applies to entities whose equity investment at risk is insufficient to finance that entity's activities without receiving additional subordinated financial support provided by any parties, including equity holders, or where the equity investors (if any) do not have a controlling financial interest. FIN No. 46R provides that if an entity is the primary beneficiary of a VIE, the assets, liabilities, and results of operations of the VIE should be consolidated in the entity's financial statements. In addition, FIN No. 46R requires that both the primary beneficiary and all other enterprises with a significant variable interest in a VIE provide additional disclosures. The provisions of FIN No. 46R became effective in the first quarter of fiscal 2004. The adoption of FIN No. 46R did not have a material impact on our financial position or our results of operations.

Quantitative and Qualitative Disclosure of Market Risks

Our exposure to market risk is limited primarily to interest income sensitivity, which is affected by changes in the general level of United States interest rates, particularly because the majority of our investments are in short-term debt securities.

The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. Some of the securities in which we invest may be subject to market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. For example, if we hold a security that was issued with an interest rate fixed at the then-prevailing rate and the prevailing interest rate later rises, the principal amount of our investment will probably decline. To minimize this risk, in accordance with our investment policy, we maintain our portfolio of cash equivalents, short-term marketable securities and restricted cash in a variety of securities, including commercial paper, money market funds, government and non-government debt securities and certificates of deposit. The risk associated with fluctuating interest rates is limited to our investment portfolio and we do not believe that a 10% change in interest rates will have a significant impact on our interest income. As of September 30, 2004, all of our investments were in money market accounts, certificates of deposit or investment grade corporate debt obligations and U.S. government securities.

Our exposure to market risk also relates to the increase or decrease in the amount of interest expense we must pay on our outstanding borrowings under a line of credit agreement we entered into with a financial institution in March 2003. As of September 30, 2004, this facility provides for borrowings up to \$1.0 million, of which approximately \$0.4 million is available for future borrowings. At September 30, 2004, approximately \$0.4 million was outstanding under this facility. Each borrowing under the line of credit accrues interest at the greater of the treasury note rate plus 3.0% or a fixed rate of 5.5% per annum at the date of borrowings and are repayable in 36 monthly installments. The risk associated with fluctuating interest expense is limited to this debt instrument and we do not believe that a 10% change in the treasury note rate would have a significant impact on our interest expense.

BUSINESS

Overview

We are a biotechnology company focused on the discovery, development and commercialization of drugs based on Metabolic Targeting, an approach that targets fundamental differences in metabolism between normal and certain diseased cells. We are building a pipeline of drugs that are designed to selectively target tumor cells so that the drugs are less toxic to healthy tissues than conventional drugs, thereby providing improvements over current therapies.

Our initial clinical focus is the treatment of cancer and benign prostatic hyperplasia, or BPH, a disease characterized by overgrowth of the prostate. We have three product candidates. Glufosfamide, our lead product candidate for cancer, has completed two Phase 1 and five Phase 2 clinical trials in patients with various solid tumors. In September 2004, we initiated a pivotal Phase 3 clinical trial of glufosfamide for the second-line treatment of pancreatic cancer. We have received a special protocol assessment from the FDA for this trial. In addition, glufosfamide for the treatment of refractory pancreatic cancer has received fast track designation by the FDA. TH-070, our lead product candidate for the treatment of symptomatic BPH, has completed enrollment in a Phase 2 clinical trial, and we are evaluating interim data. We plan to initiate a registrational program for TH-070 to treat symptomatic BPH in the first half of 2005. Our third product candidate, 2-deoxyglucose, or 2DG, for the treatment of solid tumors, is being evaluated in a Phase 1 clinical trial as a combination therapy, which means it is administered in conjunction with other chemotherapy treatments. We are also working to discover drug candidates that are activated under the metabolic conditions typical of cancer cells, and we have identified lead compounds with promising *in vitro* data. In addition, we are investigating additional compounds for activity against BPH.

For the treatment of cancer, we believe that our product candidates, based on Metabolic Targeting, can be broadly applied to the treatment of most solid tumors and have the potential to significantly increase the effectiveness of existing therapies. Metabolic Targeting provides the opportunity to treat not only rapidly dividing tumor cells, which are targeted by chemotherapy and radiation, but also slowly dividing tumor cells that generally evade these traditional therapies and ultimately contribute to relapse. For the treatment of BPH, we believe that Metabolic Targeting will enable us to develop a new class of drugs to treat the disease more rapidly and effectively, with fewer side effects than current therapies. We believe that our focus on Metabolic Targeting, combined with our expertise in medicinal chemistry and drug development, provides us with the capability to identify, discover and develop novel therapies.

Our product candidates are focused on treating patients with significant unmet medical needs. Cancer is the second leading cause of death in the United States after cardiovascular disease. The American Cancer Society estimates that 563,700 people will die from cancer in the United States this year. Many cancers, such as pancreatic, lung and liver cancer, have few effective treatments and very low survival rates. BPH, which often leads to debilitating urinary problems, affects 50% of men in their sixties and approximately 90% of men over seventy, and current treatments have significant deficiencies. Approximately 17 million men in the United States, 27 million men in five major European countries and eight million men in Japan are estimated to suffer from symptoms of the disease and could benefit from a safe and effective treatment for BPH.

Limitations of Conventional Therapies

Current Therapies for Cancer

Many different approaches are used in treating cancer, including surgery, radiation and drugs or a combination of these approaches. Drugs used to treat cancer include chemotherapeutics, hormones and immune-based therapies. Traditionally, strategies for designing cancer therapies have focused on killing cancer cells that exhibit rapid division and growth, and most conventional cancer drugs have been evaluated and optimized using cellular and animal models that reflect rapid cell growth. However, most solid tumors are actually composed of both rapidly and slowly dividing cells. Conventional cancer treatments are not designed to target the slowly

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dividing cells found in large portions of solid tumors and therefore rarely succeed in killing all cancerous cells. These slowly dividing cells, which can evade treatment, often contribute to relapse.

Another disadvantage of current cancer therapies that target rapidly dividing cells is their toxic side effects. Because rapidly dividing cells are also found in many healthy tissues, particularly the gastrointestinal tract, bone marrow and hair follicles, nearly all conventional chemotherapy drugs cause severe side effects, such as diarrhea and reduction in blood cell production, which may lead to bleeding, infection and anemia, as well as other side effects, such as hair loss. Likewise, radiation generally cannot be administered without causing significant damage to healthy tissue surrounding a tumor. The toxic and potentially fatal side effects of chemotherapy and radiation therapy are controlled by carefully balancing dose and dosing schedules to minimize toxicity to healthy cells and maximize cancer cell death. Unfortunately, achieving such a balance may permit rapidly dividing cancer cells to survive treatment, resulting in inadequate therapy.

Current Therapies for BPH

BPH is currently treated with drugs and, if necessary, surgery. There are two classes of drugs to treat BPH. The first, alpha adrenergic receptor blockers, work by relaxing the smooth muscle in the urethra and bladder without addressing the underlying condition of the enlarged prostate. Drugs in the second category, 5-alpha reductase inhibitors, work by blocking production of the hormones that stimulate the growth of new prostate cells but do not immediately kill existing cells. Consequently, this class of drugs has a slow onset, typically requiring daily treatment for many months before improving patient symptoms. Drugs in both classes can have significant side effects, including decreased libido, impotence and cardiovascular effects. Many patients ultimately fail existing medical therapy, leading to 350,000 surgical procedures annually in the United States, despite the risks of serious surgical complications including impotence and incontinence. The deficiencies in current therapies provide an opportunity for new drugs with improved efficacy or reduced side effects.

Metabolic Targeting

Metabolic Targeting is a therapeutic approach that targets fundamental differences in energy metabolism between normal and certain diseased cells. Cells generate energy needed for survival in two ways: the citric acid cycle and glycolysis. The citric acid cycle is a highly efficient process which provides the majority of cellular energy under normal conditions. Oxygen is essential for energy production through the citric acid cycle. Glycolysis, also called glucose metabolism, is the process by which glucose is converted to energy and is much less efficient in producing energy than the citric acid cycle. Unlike the citric acid cycle, oxygen is not required for glycolysis, and cells that rely primarily on glycolysis for energy production consume large quantities of glucose. Some diseased cells rely predominantly or exclusively on glycolysis. When these cells shift energy production to glycolysis, they must increase the levels of the proteins needed to transport and metabolize glucose. Metabolic Targeting takes advantage of these metabolic differences to selectively target certain diseased cells.

Metabolic Targeting For Cancer

Cancer cells require large amounts of glucose for energy production and growth. This increased consumption of glucose has two causes: the process of a normal cell becoming a rapidly dividing cancer cell; and the exposure of a cell to the low oxygen conditions, also called hypoxia, within those regions of most solid tumors where cells are dividing slowly. First, when cells become cancerous, they require more energy and the level of proteins needed for glucose transport and metabolism increases. Second, as a tumor grows, it rapidly outgrows its blood supply, leaving portions of the tumor with regions where the oxygen concentration is significantly lower than in healthy tissues. As a consequence, tumor cells in these hypoxic zones rely on glycolysis for energy production and therefore further increase the levels of proteins responsible for glucose transport and metabolism.

We are focused on developing new cancer therapies by targeting the intake and metabolism of glucose by cells. In one application of Metabolic Targeting, we use a cancer-killing drug linked to glucose to take advantage of

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increased glucose transport proteins of cancer cells, thereby delivering the drug selectively to these cancer cells. In another application of Metabolic Targeting, we use compounds that interfere with specific steps of glycolysis. Because cancer cells depend on glycolysis to survive, these compounds substantially reduce energy production, leading to cell death. We are also pursuing drugs that incorporate both of these applications of Metabolic Targeting.

We believe that our product candidates may prove effective for treating rapidly dividing cancer cells because these cells require large amounts of energy and thus metabolize more glucose than do normal cells. Glufosfamide targets the increased glucose transport by these cells through linking a cancer-killing drug to glucose, which enters these cells at relatively higher levels compared to most normal cells. Our other product candidates target glucose metabolism directly and provide the opportunity to increase the effectiveness of current therapies that treat the rapidly dividing cells in the tumor by reducing energy production in those cells. Radiation therapy, as well as the vast majority of chemotherapy drugs, kill cells by damaging DNA or affecting DNA synthesis to prevent cell replication. However, highly energy-dependent DNA repair mechanisms can restore the integrity of a cell's DNA. The balance between the extent of DNA damage and the efficiency of cellular DNA repair thus largely determines the effectiveness of therapy. Our product candidates that reduce cellular energy production inhibit these repair mechanisms, shifting the balance from repair to damage, and may increase the efficacy of current treatments. Furthermore, cancer cells become resistant to many conventional chemotherapy drugs by a highly energy-dependent process that pumps these drugs out of the cell, reducing their effect. Our product candidates that interfere with cellular energy production can disrupt this multidrug resistance, resulting in increased chemotherapy drug accumulation within the cell, which we believe will increase the effectiveness of these chemotherapy drugs.

In addition to treating rapidly dividing cancer cells, we believe that Metabolic Targeting provides the opportunity to kill slowly dividing cancer cells within hypoxic regions, which are poorly treated by current therapies that primarily target the rapidly dividing cells. Cell proliferation in hypoxic regions is greatly inhibited due to poor blood supply leading to insufficient nutrient supply and a lack of oxygen. Slowly dividing cells within the hypoxic region also undergo genetic changes which, as they accumulate in cells, can lead to the development of still more aggressive tumor cells that are resistant to therapy. Following treatment with radiation or chemotherapy, rapidly dividing cells in the vicinity of blood vessels are destroyed, providing room for these more aggressive cells from hypoxic regions to gain access to blood vessels and oxygen. These cells, which have become resistant to treatment, are then able to grow and proliferate, ultimately contributing to relapse. Thus, current cancer therapies leave the slowly proliferating cells in the hypoxic zones largely untreated while our product candidates are designed to kill these slowly dividing cells by targeting their increased glucose transport and metabolism.

Metabolic Targeting For BPH

We are also using Metabolic Targeting to develop a new class of drugs for BPH that may offer an improvement over current treatments. BPH is an overgrowth of prostate cells that results in a tumor that can restrict urine flow and cause a number of debilitating symptoms. Like hypoxic cancer cells, prostate cells in BPH tissue depend on glycolysis for energy production. These cells divert citrate, a molecule required for energy production by the citric acid cycle, into the seminal fluid to support the sperm, and therefore these cells cannot produce energy from the citric acid cycle. This process is mediated by the accumulation of high levels of zinc, which blocks citrate metabolism and disables the citric acid cycle in these prostate cells. These cells are therefore highly dependent on glycolysis for energy production. We are focused on developing new BPH therapies by targeting the metabolism of glucose by prostate cells. Preclinical studies and our interim Phase 2 data suggest that our product candidate TH-070 inhibits glycolysis and kills prostate cells disproportionately since normal cells can rely on the citric acid cycle for energy production. Current therapies either address BPH symptoms without addressing the underlying condition, or block growth of new prostate cells without reducing prostate size. We believe our product candidate treats both the symptoms of BPH and underlying condition as well as reduces prostate size.

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Our Product Development Programs

The following table summarizes the status of our product development programs:

Product Candidate/Indication	Development Status	Expected Milestones
Glufosfamide for Pancreatic Cancer		
• Second-line single-agent	Phase 3 in progress	Enrollment complete 1Q06
• First-line in combination with Gemzar	Phase 1/2 in progress	Phase 1 data 4Q05
TH-070		
• BPH	Phase 2 interim data available	Initiate registrational program 1H05
2-Deoxyglucose (2DG)		
• Various solid tumors	Phase 1 in progress	Results by 3Q05

Glufosfamide

Our lead product candidate for cancer, glufosfamide, is a small molecule in clinical development for the treatment of pancreatic cancer. In September 2004, we initiated a pivotal Phase 3 trial to support marketing approval of glufosfamide for the second-line treatment of metastatic pancreatic cancer. As part of our registration and approval strategy, in December 2004 we also initiated a Phase 1/2 clinical trial to evaluate various doses of glufosfamide in combination with Gemzar for the first-line treatment of inoperable locally advanced or metastatic pancreatic cancer. Animal data suggest that glufosfamide and Gemzar may work together to kill cancer cells with greater efficacy than either drug alone, without additional side effects. We believe that the unique mechanism of action of glufosfamide and its demonstrated activity in combination with Gemzar in animal studies make it well-positioned to be used in combination with Gemzar. We are developing glufosfamide for pancreatic cancer based on activity seen in previous clinical trials, a known increase in glucose uptake in pancreatic cancer cells and the extreme hypoxia in tumors of this type. In Phase 1 and Phase 2 clinical trials, glufosfamide also has shown activity in advanced stage colon cancer, non-small cell lung cancer and relapsed breast cancer but not a type of brain tumor called glioblastoma, and we believe it may offer an improvement over conventional therapies for these indications.

Glufosfamide combines the active part of an approved alkylator, a member of a widely used class of chemotherapy drugs, with a glucose molecule. Because of its glucose component and a tumor cell's increased need for glucose, glufosfamide is preferentially transported into tumors compared to most normal tissues. Thus Metabolic Targeting offers the potential to provide increased selectivity for tumor cells and thereby improve the treatment of many solid tumors. Inside cells, the linkage between glucose and the alkylator is cleaved to release the active drug. With glucose as the side product, glufosfamide has fewer side effects than other drugs in its class, which are known to cause hemorrhagic cystitis, a serious condition characterized by severe bladder bleeding.

Market Opportunity

The American Cancer Society estimates that 31,860 patients will be diagnosed with pancreatic cancer in the United States in 2004, and approximately 31,270 patients will die from the disease. Only 15-20% of newly diagnosed patients are eligible for surgery, which is typically followed by radiation and chemotherapy. Patients with inoperable pancreatic cancer are treated with radiation and chemotherapy, or in the case of advanced disease, chemotherapy alone as the advantages of radiation are reduced. Gemzar is the standard of care for the first-line therapy of advanced metastatic pancreatic cancer. The largest published trial of Gemzar in advanced pancreatic cancer reported a median survival of 5.4 months. In Gemzar's Phase 3 registrational trial, median survival was 5.7 months, and no patient survived beyond two years. In this study, patients treated with 5-flurouracil, or 5-FU, the previous standard of care, had a median survival of 4.2 months, and no patient

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survived beyond two years during the study. None of the 126 patients treated in both arms of this study achieved tumor shrinkage. Estimated worldwide 2003 sales of Gemzar for pancreatic cancer were \$422 million.

Prior Clinical Trials

Glufosfamide has been evaluated in two Phase 1 and five Phase 2 clinical trials that together enrolled over 200 patients with a variety of advanced-stage cancers. In the two Phase 1 trials, escalating doses of glufosfamide were administered to 72 patients with solid tumors not amenable to established treatments. Although Phase 1 trials are designed primarily to assess safety, tumor shrinkage was observed in patients with breast cancer, non-small cell lung cancer, pleural mesothelioma, renal cell carcinoma and cancers of unknown primary origin.

In the Phase 1 trials, the one patient with advanced pancreatic cancer achieved a complete remission, and more than five years after being treated with glufosfamide alone, this patient remained alive and disease-free. This example may not be representative of the activity of glufosfamide when studied in larger trials.

The five Phase 2 studies of glufosfamide were multi-center studies to evaluate tumor response in patients with locally advanced or metastatic pancreatic cancer, relapsed non-small cell lung cancer, a type of brain cancer called glioblastoma, locally advanced or metastatic colon cancer not amenable to surgery and relapsed metastatic breast cancer. Glufosfamide was well tolerated and showed anti-tumor activity against breast, colon, non-small cell lung and pancreatic cancers, but not glioblastoma.

In the Phase 2 trial in patients with advanced pancreatic cancer, two of 34 patients achieved a partial response (defined as 30% or greater tumor diameter shrinkage) and 11 of 34 patients achieved stable disease (defined as less than 30% tumor diameter shrinkage and less than 20% growth in tumor diameter). Overall median survival with glufosfamide was estimated at 5.6 months, and two-year survival was estimated at 9%. The preliminary results of this study, published in the *European Journal of Cancer* in November 2003, reported a median survival of 5.3 months.

In the Phase 1 and Phase 2 trials, glufosfamide was generally well tolerated, with few drug-related serious adverse events. In particular, glufosfamide's adverse effects on bone marrow and the kidneys were generally reversible without requiring treatment of the side effects. Only 1% of patients developed severe lowering of the blood platelets, which help to stop bleeding. Toxicity to the kidney, as measured by serum elevation in waste products normally excreted by the kidney, was severe in only 1% of patients. Nausea and vomiting is the most common side effect of glufosfamide treatment. There have been no reports of hemorrhagic cystitis in patients treated with glufosfamide.

The Phase 1 and Phase 2 trials of glufosfamide were conducted by ASTA Medica Oncology, which was subsequently acquired by a subsidiary of Baxter International. We exclusively licensed worldwide rights to the compound and associated clinical data from Baxter.

Ongoing Clinical Programs

We are planning to develop glufosfamide as a single agent for the second-line treatment of metastatic pancreatic cancer, and in combination with Gemzar for the first-line treatment of inoperable, locally advanced and/or metastatic pancreatic cancer. In September 2004, we initiated a pivotal Phase 3 trial of glufosfamide for the treatment of patients with metastatic pancreatic cancer who have failed treatment with Gemzar. This two-arm trial will compare glufosfamide to best supportive care, since there is no approved second-line treatment for pancreatic cancer. The final trial design will call for enrollment of approximately 300 patients. For its primary endpoint, this trial will compare the survival of patients treated with glufosfamide to patients who receive only best supportive care. We have received a special protocol assessment from the FDA for this trial. The special protocol assessment is a process that allows for official FDA evaluation of the proposed design of a Phase 3 clinical trial. It provides trial sponsors with an agreement on trial design and analysis required to support a new

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drug application submission, if the study is performed according to the special protocol assessment and meets its primary endpoint. In addition, glufosfamide for the treatment of refractory pancreatic cancer has been granted fast track designation by the FDA. The fast track drug development program provides for expedited regulatory review for new drugs demonstrating the potential to address unmet medical needs for the treatment of serious life-threatening conditions. Moreover, the FDA will facilitate and expedite the development and review of the application for drugs in the fast track program.

As part of our registration and approval strategy, in December 2004 we also initiated a Phase 1/2 trial to evaluate glufosfamide in combination with Gemzar for the first-line treatment of advanced pancreatic cancer patients. The trial will evaluate various doses of glufosfamide in combination with the standard dose of Gemzar. The Phase 1 portion of this trial will enroll 15 patients with a variety of solid tumors for which Gemzar is currently used to establish the maximum tolerated dose of glufosfamide when administered with Gemzar. The Phase 2 portion is intended to determine the clinical activity of this combination. We anticipate that approximately 47 patients will be enrolled in the Phase 2 portion of this trial.

Even though our immediate efforts will be focused on pancreatic cancer, the results of Phase 1 and Phase 2 clinical trials suggest that glufosfamide may also be useful for the treatment of other cancers. We expect to initiate additional glufosfamide clinical trials for other indications. Based on human clinical data, the activity of approved alkylators and our understanding of the mechanism of action of glufosfamide, we believe that breast, lung and colon cancers, as well as lymphomas and sarcomas, represent the most promising indications.

TH-070

TH-070, our lead product candidate for the treatment of symptomatic BPH, is an orally administered small molecule that has been reported to inhibit glycolysis by inactivating hexokinase, the enzyme that catalyzes the first step in glycolysis. As described above, hypoxic tumor cells and certain prostate cells depend on glycolysis for their energy production. By inhibiting glycolysis, TH-070 kills prostate cells, reducing the size of the prostate, and therefore may provide an effective treatment for symptomatic BPH. We have completed enrollment and are evaluating interim clinical data from a Phase 2 trial of TH-070 for the treatment of symptomatic BPH. We plan to initiate a registrational program for this indication in the first half of 2005. We initially selected TH-070 to treat BPH based on our understanding that prostate cells rely predominantly on glycolysis for energy production as well as published animal data and human clinical data demonstrating tolerability.

BPH Market Opportunity

As a man ages, it is common for his prostate to enlarge. This enlargement process begins as early as age 25 but does not cause problems until later in life, when the prostate presses against the urethra and symptoms of BPH become evident. Because the prostate surrounds the urethra, BPH can restrict the flow of urine, resulting in urine retention, which can cause weakening of the bladder wall and the inability to empty the bladder completely. The most common symptoms of BPH include a weak and interrupted urine stream, urgency, leaking and frequent urination. Severe BPH can result in urinary tract infections, kidney and bladder damage, bladder stones and incontinence.

The National Institutes of Health, or NIH, estimates that more than 50% of men in their sixties and approximately 90% of men over seventy have some symptoms of BPH. Approximately 17 million men in the United States, 27 million men in five major European countries and eight million men in Japan are estimated to suffer from symptoms of the disease and could benefit from a safe and effective treatment for BPH. Approximately 21% of them have been diagnosed, of which 59% receive medical therapy. In the United States, 2.0 million men are treated with drugs. These numbers are expected to increase in the future due to increased awareness and the aging population.

The two major drugs approved to treat BPH, Flomax and Proscar, had combined worldwide revenues of over \$1.6 billion in 2003. Alpha adrenergic receptor blockers, such as Flomax, work by relaxing the smooth muscle in the urethra and bladder and do not change the size of the prostate. In clinical studies of Flomax for the

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treatment of BPH symptoms, the average increase in urine flow was approximately 1.8 mL/sec. after four weeks of treatment. 5-alpha reductase inhibitors, such as Proscar and recently approved Avodart, work by blocking production of the hormones that stimulate the growth of new prostate cells but do not immediately kill existing cells. Consequently, this class of drugs has a slow onset, typically requiring daily treatment for many months before improving patient symptoms. In clinical studies of Avodart, the average increase in urine flow was approximately 0.8 mL/sec. and the average decrease in prostate size was approximately 8% after four weeks of treatment.

TH-070 offers the potential to treat symptomatic BPH via a novel mechanism, by reducing the prostate size through Metabolic Targeting. By directly inhibiting glycolysis in prostate cells, we expect TH-070 to reduce the size of the prostate more rapidly than current medical treatments, without the attendant side effects, which include decreased libido, impotence and cardiovascular effects.

Prior Clinical Trials and Preclinical Studies

Studies have shown that, at the highest doses studied, multiple TH-070 doses can shrink the rat prostate by over 40%, and a single oral dose of a TH-070 analog can reduce the size of the rat prostate by up to 24%. Prostate shrinkage occurs at dosages that cause no observable adverse clinical effect on the animals and can be seen within ten days of dosing.

Ongoing Clinical Program

In January 2004, we initiated a Phase 2 clinical trial managed by PPD Development, L.P. and PPD Global Limited, at the University of Bari, Italy, to evaluate the safety and efficacy of TH-070 in patients with symptomatic BPH. This trial is an open-label, two-arm study designed to enroll a total of 60 patients in two 30-patient dosing schedules of TH-070, 150 mg once a day and 150 mg three times a day. These doses and dosing schedules were based on animal efficacy data as well as human safety data. Based on promising interim data from the low-dose group of patients in this study, we elected not to enroll the high-dose group and instead plan to initiate a registrational program for TH-070 to treat symptomatic BPH in the first half of 2005.

In our Phase 2 trial, patients are being evaluated at several dates for specific efficacy variables, including prostate size, maximum urine flow rate, prostate specific antigen levels, or PSA, and an assessment of each patient's BPH symptoms called the International Prostate Symptom Score, or IPSS. IPSS is a clinically validated seven question, self-administered questionnaire to assess lower urinary tract symptoms. These efficacy variables include those that have been used as endpoints in previous clinical trials that led to FDA approval of currently marketed BPH drugs. The primary endpoint specified in the protocol for our trial is a comparison of prostate size between baseline and day 28 of treatment.

In the trial we observed statistically significant improvements in all variables measured by day 14 of treatment, and further improvements by day 28. All p-values were less than 0.005, except for day 14 PSA levels. A p-value is a statistical term that indicates the probability that a desired result is random. The smaller the p-value, the lower the likelihood that the desired result was random. A p-value of 0.05 or less is considered statistically significant. These interim results are shown in the table below.

	Percentage Change from Baseline			
	Prostate Size	Maximum Urine Flow Rate	IPSS	PSA
Day 14	- 7.4%	+33.0%	not determined	- 2.7%
Day 28	-13.5%	+47.9%	-44.2%	-24.3%

In particular, at day 28 of treatment the average decrease in prostate size was 7.1 cc (-13.5%), the average increase in maximum urine flow rate was 4.5 mL/sec. (+47.9%), the average decrease in IPSS was 8.4 units (-44.2%) and the average decrease in PSA levels was 0.9 ng/mL (-24.3%). TH-070 was well tolerated with no

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therapy-related side effects. We continue to follow all patients enrolled and treated in the trial and will do so for a period of six months from first treatment. The purpose of looking at longer-term data is to determine whether the improvements are sustained after the treatment regimen has been completed.

We expect to publish detailed results of this trial in the second quarter of 2005. Based on the interim results, we intend to initiate a registrational program of TH-070 for the treatment of symptomatic BPH in the first half of 2005. Our registrational program will include multiple multicenter, randomized, double-blinded, placebo-controlled studies, including at least one dose-comparison study. Although our final trial design is not complete, in future clinical trials we expect to measure the same variables we are measuring in our current Phase 2 trial. We expect to commence two clinical trials in the first half of 2005, at least one of which should be a Phase 3 trial. There can be no assurance that regulatory authorities will consider these studies pivotal, and we expect our registrational program to include additional trials.

2-Deoxyglucose (2DG)

2DG, our product candidate for the treatment of solid tumors, is in a Phase 1 trial. 2DG is an orally administered small molecule that employs Metabolic Targeting to treat solid tumors by directly inhibiting glycolysis. Because tumor cells in general, and those in hypoxic zones in particular, are dependent on glycolysis for survival, tumor cells are particularly sensitive to the effect of 2DG. This compound is a synthetic glucose analog that distributes selectively to tumor tissue because of metabolic changes related to increased glucose consumption. Because tumor cells exhibit increased levels of glucose transport proteins, these cells actively transport 2DG into the cells. Once inside the cell, 2DG interferes with cellular mechanisms for generating energy by competing with glucose for key enzymes in glycolysis. The *in vivo* efficacy of 2DG has been studied in mouse and rat models of certain cancers, including sarcomas, adenocarcinomas, leukemias, melanomas and bladder, colon and breast tumors. In particular, treatment with 2DG, alone and in combination with other chemotherapy, resulted in increased lifespan or a reduction in tumor growth in many of these models.

We are conducting a Phase 1 trial of daily 2DG as a single agent and in combination with Taxotere to evaluate the safety, blood levels and maximum tolerated dose in patients with solid tumors. Animal studies suggest that 2DG and Taxotere may work together to kill cancer cells with greater efficacy than either drug alone, without increased risk of side-effects. We plan to also conduct a Phase 1 trial of single doses of 2DG to evaluate its effect on prostate metabolism. We are developing 2DG based on its specificity for targeting tumor cells and extensive human safety data, as well as recently demonstrated animal efficacy that we and our collaborators at the University of Miami published in *Cancer Research* in January 2004.

Clinical Trials

2DG has been administered in clinical trials to approximately 700 people principally to evaluate the hormonal and metabolic effects of glucose deprivation. Collectively, these studies have shown that single intravenous doses of 2DG as high as 200 mg/kg do not cause any serious adverse events. Although this data supports the safe use of 2DG in humans, we have not yet obtained human safety data for the cumulative dose or oral administration of 2DG we intend to use in our clinical trials. The FDA may require such data before allowing us to proceed into pivotal clinical trials that will support approval.

We launched a Phase 1 clinical trial of 2DG in January 2004 at the University of Miami and have initiated a second site at the Cancer Therapy and Research Center, located in San Antonio, Texas. This trial is a dose-escalation study to determine the safety, blood levels and maximum tolerated dose of daily oral doses of 2DG given alone or in combination with Taxotere. The study is intended to enroll up to 50 patients with previously treated refractory advanced solid tumors. The study will also evaluate the effect of 2DG alone and in combination with Taxotere on tumor metabolism, and provide a preliminary assessment of efficacy, as assessed by computer tomography. We expect initial data from the study to be available by the third quarter of 2005.

Provided our safety study yields favorable results, we are planning to initiate Phase 2 studies that will be randomized, blinded, multiple-dose studies designed to evaluate the safety and efficacy of 2DG given in

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combination with chemotherapy. We will choose two indications and appropriate chemotherapy drugs for our Phase 2 program based on the results of the ongoing Phase 1 trial.

We plan to conduct a second Phase 1 trial of a single dose of 2DG in patients with prostate cancer. This study will evaluate the biological effect of 2DG on metabolism in the prostate. This study will provide additional data on the safety, tolerability and blood levels of 2DG.

Discovery Research

We have research programs focused on the design and development of novel cytotoxic prodrug compounds. A prodrug is an inactive compound that is converted in the human body either by spontaneous chemical reactions or enzymatic processes that result in the formation of an active drug. The prodrug concept is well established in chemotherapy, but it was initially only employed to modify the pharmacokinetic properties of compounds through non-specific activation processes. Only more recently has the concept been put to use in the design of agents that are selectively activated in tumor tissues through specific activation processes.

Our prodrugs have two distinct parts, a toxic portion and an attached trigger molecule. To prevent general toxicity, the trigger molecule masks the toxin until the prodrug is activated by low oxygen concentration in the target tissue. Once activated, the toxin kills cells in its vicinity. We have designed prodrugs that are triggered only at the very low oxygen levels found in the hypoxic regions of solid tumors. Our experiments indicate that we can achieve a greater than 100-fold difference in cytotoxicity between cells in normal oxygen levels and hypoxic cells. We have identified lead compounds with promising *in vitro* data, and additional characterization, evaluation and optimization of these compounds is currently underway.

In addition, we have an active effort to develop new formulations of TH-070 and identify additional compounds suitable for development as BPH products. Our efforts include de novo compound discovery, as well as evaluation of existing compounds.

Our expertise includes broad capabilities in target identification and validation, assay development and compound screening. Our medicinal chemistry expertise includes the use of state-of-the-art technologies to turn initially promising compounds generated by our chemists into drug candidates. We believe that our research focus combined with our medicinal chemistry expertise provide us with the capacity to identify, discover and develop novel therapies.

Our Strategy

Our goal is to create a leading biotechnology company that develops and commercializes drugs based on Metabolic Targeting with an initial focus on cancer and BPH. Key elements of our strategy are to:

- *Develop glufosfamide, TH-070 and 2DG successfully.* For glufosfamide, we have an ongoing Phase 3 trial for the second-line treatment of metastatic pancreatic cancer and an ongoing Phase 1/2 trial for the first-line treatment of inoperable locally advanced or metastatic pancreatic cancer. For TH-070, we have an ongoing Phase 2 trial for the treatment of symptomatic BPH and expect to begin two Phase 3 trials for the treatment of symptomatic BPH in the first half of 2005. For 2DG, we have an ongoing Phase 1 trial to evaluate the safety, blood levels and maximum tolerated dose in patients with solid tumors. We intend to advance all of our clinical programs as aggressively as possible, and assuming clinical results are positive, expect to file NDAs with the FDA and other foreign regulation agencies for our two lead product candidates, glufosfamide and TH-070, within three years. We are also exploring additional indications for these product candidates.
- *Continue to broaden our pipeline by identifying, discovering and developing new compounds.* We are actively pursuing a focused research program based on Metabolic Targeting to discover and develop

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novel therapies that address major unmet medical needs. We also plan to continue to evaluate additional in-licensing opportunities that build on our expertise and complement our current development pipeline.

- *Build on our expertise in Metabolic Targeting through continued research in cellular metabolism.* We intend to continue our focused approach in research and clinical development. We believe our expertise in Metabolic Targeting gives us an advantage in the identification of new product candidates, therapeutic indications and technologies. We will also leverage the expertise of our scientific and clinical advisors and continue to enter into collaborations with other experts in the field.
- *Develop sales and marketing capabilities in select markets.* We intend to retain commercial rights to our products for indications and territories where we believe we can effectively market them. For all other indications and territories, we intend to pursue strategic collaborations.

Manufacturing and Supply

The production of glufosfamide, TH-070 and 2DG employs small molecule organic chemistry procedures that are standard for the pharmaceutical industry. We currently rely on contract manufacturers for the manufacture of API and final drug product of glufosfamide, TH-070, 2DG, and any other products or investigational drugs for development and commercial purposes. We intend to continue to use our financial resources to accelerate the development of our product candidates rather than diverting resources to establishing our own manufacturing facilities.

We currently have sufficient supplies of glufosfamide drug product to conduct and complete our planned clinical trials, which have been prepared by a subsidiary of Baxter International, Inc. Our supply of glufosfamide has been stable for the past two years; however, should our current supply not remain stable, we may experience a significant delay in the completion of our pivotal Phase 3 trial. We are in the process of qualifying back-up vendors to manufacture glufosfamide API and drug product, although we may not be able to do so at acceptable cost or terms, if at all.

We believe that we have sufficient supplies of TH-070 API to conduct and complete our two currently planned BPH clinical trials. We have ordered additional TH-070 API from Jiangsu Hengrui Medicine Company, Ltd. We have recently entered into an agreement with Pharmaceutics International, Incorporated for manufacture of TH-070 drug product. We have not yet received any API or drug product from these manufacturers. The failure of Pharmaceutics International to meet quality requirements or otherwise perform its obligations could significantly delay our TH-070 clinical program. In addition, failure of Jiangsu Hengrui Medicine Company to provide acceptable API could delay commercialization of TH-070, if approved.

We believe that we have a sufficient supply of 2DG for our anticipated clinical trials over the next two years, although there can be no assurance that these supplies will remain stable and usable during this period. If these materials are not stable, we may experience a significant delay in our 2DG clinical program.

Sales and Marketing

We intend to build our own sales force to market our cancer drugs and to maintain all commercial rights to our cancer products in the United States and potentially in Europe. Because the United States cancer market is relatively concentrated, we believe we can effectively target it with a small specialized sales force. We may pursue strategic collaborations to commercialize our products in other territories for cancer and on a worldwide basis for indications treated by large physician populations, such as BPH. We currently have no marketing, sales or distribution capabilities. In order to commercialize any of our drug candidates, we must develop these capabilities internally or through collaborations with third parties.

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License and Development Agreements

TH-070 License

In June 2004, we entered into an agreement with Acraf, S.p.a., for rights to use Acraf's regulatory documents and pre-clinical and clinical information pertaining to the active ingredient in TH-070 for our regulatory filings on TH-070-based products and for obtaining marketing authorizations world-wide for such products. Our license is exclusive in territories other than specified European Union countries, including France, Germany, Great Britain, Italy, Portugal, Spain and Hungary, certain eastern European countries and certain countries in the former Soviet Union, which we call the Acraf Territory. In the Acraf Territory, our rights are non-exclusive. Additionally, under the agreement, Acraf will own all intellectual property rights with respect to the information licensed to us and we will own the intellectual property rights to any data that we obtain from our clinical trials related to anti-cancer activity pursuant to an agreed-upon development plan and, to the extent we conduct trials for certain cancer indications, we granted Acraf a co-exclusive license to use such data and any patents thereon in the Acraf Territory for purposes of supporting use of TH-070 for cancer indications.

In consideration for our licenses under this agreement, we paid Acraf a one-time payment of €300,000, or approximately \$374,000. We will also pay Acraf milestone payments, with the next such milestone payment due in connection with the marketing approval of our first TH-070-based product in certain territories. In addition, there is a sales-based milestone due when sales of a TH-070 containing Threshold product exceed €50 million in one year. Future aggregate milestone payments could total €1.8 million. We have also agreed to use reasonable business efforts to determine whether development of TH-070 for other cancer indications should be pursued.

We purchased from Acraf 22 kilograms of active ingredient of TH-070 for a purchase price of €75,000. We also granted Acraf a first right to manufacture and supply 75 percent of the TH-070 active ingredient that we require on terms that are no less favorable than we could obtain from a third-party supplier. Acraf's supply right begins in June 2006 and extends for 10 years from the date of our first launch of our TH-070-based products unless Acraf fails to meet the terms offered by a third-party supplier, in which case Acraf's supply right will terminate.

Our licenses from Acraf under the agreement extend for fifteen years from the date of our first launch of the first TH-070-based products in exclusive territories. Acraf's licenses under the agreement extend for fifteen years following Acraf's first launch of any product in the Acraf Territory. The agreement may not be terminated by either party except for failure to perform due to events beyond a party's control and which cannot be overcome.

Glufosfamide License

In August 2003, we entered into an agreement with Baxter International, Inc. and Baxter Healthcare S.A., together Baxter, for the licensing and development of glufosfamide. Under this agreement, we have an exclusive worldwide license and/or sublicense under Baxter's patent rights, proprietary information and know-how relating to glufosfamide to develop and commercialize products containing glufosfamide for the treatment of cancer. Baxter's patent rights include one issued United States patent and 24 foreign counterparts related to glufosfamide, as well as one foreign patent related to its manufacture. Baxter has agreed to provide us with all of its information related to glufosfamide, including animal study data.

In consideration for our licenses under this agreement, we paid an upfront license fee of \$100,000 and development milestone payments of \$100,000 and \$1.3 million. We are obligated to make certain additional development milestone payments, with the next such payment due in connection with the filing of a new drug application with the FDA for glufosfamide. Future milestone payments in connection with the development of glufosfamide and United States and foreign regulatory submissions and approvals could equal \$8.0 million, and sales-based milestone payments could total up to \$17.5 million. Following regulatory approval, we will be obligated to pay royalties to Baxter based on sales of glufosfamide products.

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This agreement remains in effect until terminated by either party. We may terminate the agreement at will upon 60 days prior written notice to Baxter. Baxter may terminate this agreement if we:

- fail to meet our obligations under the agreement to develop and commercialize a glufosfamide product and we have not cured this breach within 90 days after receiving a notice from Baxter;
- discontinue development of glufosfamide products for a continuous period of 12 months, in a manner that is inconsistent with our then-current plan to develop glufosfamide products, and we have not cured this breach within 90 days after receiving a notice from Baxter;
- are in material breach of any other term of the agreement, which is not cured within 60 days of any notice by Baxter; or
- become insolvent.

Glufosfamide Asian Development Agreement

In November 2004, we entered into a Development Agreement with MediBIC Co. Ltd. MediBIC is a publicly traded Japanese biotechnology company focused on developing therapeutic compounds in partnership with non-Japanese biotechnology firms and providing consulting services in the design, management and data analysis of clinical trials using pharmacogenomic platforms developed internally and in collaboration with other companies. By working with MediBIC, we believe that we will be able to develop glufosfamide in Asian countries more quickly than by undertaking such efforts on our own or with other third parties. Pursuant to this agreement, we will work with MediBIC to create a development plan for glufosfamide for the treatment of cancer in certain Asian countries, including Japan, North Korea, South Korea, India, China, Taiwan and Hong Kong, in an indication to be determined as part of the development plan. We have also received an exclusive, royalty free license to MediBIC's know-how for the manufacture, sale and distribution of glufosfamide products for the treatment of cancer worldwide.

Under this agreement, in December 2004 we received an upfront payment of \$4.75 million to support the development of glufosfamide in the Asian countries covered by the agreement and an option payment of \$250,000. We will be required to refund these payments and the agreement will terminate if we and MediBIC cannot agree to the development plan described above by March 1, 2005, or a later date agreed by the parties. We are responsible for all development activities and MediBIC has no other funding obligations. We have agreed to pay MediBIC a percentage of net sales or net revenues from the sales of glufosfamide products for the treatment of cancer by us or third parties in the Asian countries covered by the agreement. We may also be required to pay MediBIC a percentage of up front or milestone payments we receive from any third-party sublicensee of ours for the development of a glufosfamide product for the treatment of cancer in those Asian countries. In addition, until July 1, 2005, or earlier if we terminate our agreement with MediBIC, we have agreed not to offer any party other than MediBIC the right to develop glufosfamide in the Asian countries covered by the agreement, except in connection with an acquisition of us or certain other transactions. We may terminate this restriction at any time by refunding the \$250,000 option payment to MediBIC.

Our agreement with MediBIC will terminate if we and MediBIC do not agree to a development plan as described above by March 1, 2005, or a later date agreed by the parties. We may also terminate the agreement at any time by making certain payments to MediBIC ranging from \$5.25 to \$15 million, depending on the stage of development. Otherwise, the agreement will continue until the expiration of the last-to-expire patent in a country in the Asian territories covered by the agreement that is owned or controlled by us and claims glufosfamide, its use for the treatment of cancer or a process to make such compound in such country.

2DG License

In November 2002, we entered into an exclusive license agreement with Dr. Theodore J. Lampidis and Dr. Waldemar Priebe. This agreement gives us exclusive worldwide rights to international patent application US01/07173, to all of its United States counterpart and priority applications, and any United States and foreign patents and patent applications that claim priority from such application. One United States patent licensed under

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this agreement has been issued. This patent and related pending applications cover the treatment of cancer with 2DG in combination with certain other cancer drugs.

In consideration for this license, we have reimbursed Dr. Lampidis and Dr. Priebe for patent costs and will bear all future patent costs incurred under this agreement. We are also obligated to make certain milestone payments, including milestone payments of up to \$700,000 in connection with the filing and approval of a NDA for the first product covered by the licensed patents, as well as royalties based on sales of such products. This license terminates upon the last to expire issued patent covering the technology licensed under it. We have the right to terminate the license at will upon written notice to Dr. Lampidis and Dr. Priebe.

The U.S. government funded research conducted by Drs. Lampidis and Priebe and therefore, the research is subject to certain federal regulations. For example, under the "march-in" provisions of the Bayh-Dole Act, which governs the transfer of technology developed under federal grants and contracts, the government may have the right under limited circumstances to grant licenses to the technology.

Patents and Proprietary Rights

Our policy is to patent the technologies, inventions and improvements that we consider important to the development of our business. As of September 30, 2004, we hold exclusive commercial rights to two issued United States patents, 24 issued or designated foreign counterparts of one of these patents, three foreign counterpart applications and two United States continuation applications of the other of these patents and one additional foreign patent.

Intellectual Property Related to Glufosfamide

Our glufosfamide product candidate is covered by one issued United States patent and 24 foreign counterpart patents, as well as one foreign patent relating to its manufacture. These patents are owned by Baxter, which has exclusively licensed them to us. The major European market counterparts of the United States patent expire in 2009, and the United States patent expires in 2014. Under the Hatch-Waxman Act in the United States, and similar laws in Europe, there are opportunities to extend the term of a patent for up to five years. Although we believe that our glufosfamide product candidate will meet the criteria for patent term extensions, there can be no assurance that we will obtain such extensions. Based on our current clinical timeline, if such an extension were obtained we expect that it would be for approximately three years or less. In addition, we have filed an international patent application describing methods for the identification of patients likely to be most responsive to glufosfamide therapy and a United States provisional patent application describing the use of glufosfamide in combination with gemcitabine to treat cancer.

Intellectual Property Related to TH-070

Our TH-070 product candidate for BPH is protected by one United States patent application claiming methods of treating BPH, as well as one international counterpart of this application. In addition, we have filed an international patent application that broadly claims the use of glycolytic inhibitors to treat BPH. We have also filed five provisional United States patent applications relating to TH-070 analogs and prodrugs.

Intellectual Property Related to 2DG

Our 2DG product candidate is protected by one issued United States patent claiming methods for treating breast cancer with 2DG and either paclitaxel or docetaxel (Taxotere), as well as two pending United States applications claiming the use of 2DG and other glycolytic inhibitors in combination with certain other cancer drugs, and three pending foreign counterpart applications. We have licensed exclusive commercial rights to these patents from the inventors. In addition, we own one pending United States application and its international counterpart claiming methods for dosing, administering and formulating 2DG to treat cancer.

Intellectual Property Related to Our Discovery Research

Our hypoxia-activated prodrugs are protected by one provisional United States patent application and one international patent application claiming the compounds and their use as cancer drugs.

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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 will result in the issuance of any patents. Moreover, any issued patent does not guarantee us the right to practice the patented technology or commercialize the patented product. Third parties may have blocking patents that could be used to prevent us from commercializing our patented products and practicing our patented technology. Our issued patents and those that may be issued in the future may be challenged, invalidated or circumvented, which could limit our ability or render us unable to stop competitors from marketing related products as well as shorten the term of patent protection that we may have for our products. In addition, the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that do not infringe our intellectual property rights. For these reasons, we may have competition for our products. Moreover, because of the extensive time required for development, testing and regulatory review of a potential therapeutic 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 also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive position. We seek to protect our proprietary information by requiring our employees, consultants, contractors, outside scientific collaborators and other advisors to execute non-disclosure and assignment of invention agreements on commencement of their employment or engagement. Agreements with our employees also forbid them from using third party trade secret or other confidential information in their work. We also require confidentiality or material transfer agreements from third parties that receive our confidential data or proprietary materials.

The biotechnology and biopharmaceutical industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. For so long as our product candidates are in clinical trials, we believe our clinical activities fall within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the United States, which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. This exemption does not apply to commercialization activities, however, so if our product candidates are commercialized, the possibility of a patent infringement claim against us increases. While we attempt to ensure that our clinical product candidates and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties' patents and other proprietary rights. However, there can be no assurance that they do not, and competitors or other parties may assert that we infringe their proprietary rights in any event.

Competition

We operate in the highly competitive segment of the pharmaceutical market comprised of pharmaceutical and biotechnology companies that research, develop and commercialize products designed to treat cancer. Many of our competitors have significantly greater financial, manufacturing, marketing and product development resources than we do. Large pharmaceutical companies in particular have extensive experience in clinical testing and in obtaining regulatory approval for drugs. These companies also have significantly greater research capabilities than we do. In addition, many universities and private and public research institutes are active in cancer research, some in direct competition with us. We also compete with these organizations to recruit scientists and clinical development personnel.

Competition for our Cancer Product Candidates

Each cancer indication for which we are developing products has a number of established medical therapies with which our candidates will compete. Most major pharmaceutical companies and many biotechnology companies are aggressively pursuing cancer development programs, including traditional therapies and therapies

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with novel mechanisms of action. Our glufosfamide product candidate for pancreatic cancer will compete with Gemzar, marketed by Lilly, and 5-fluorouracil, or 5-FU, a generic product which is sold by many manufacturers. Estimated worldwide 2003 sales of Gemzar for pancreatic cancer were \$422 million. In Gemzar's Phase 3 registrational trial, no patient survived beyond two years. In addition, Camptosar[®], marketed by Pfizer, and Taxotere, marketed by Aventis, are under investigation as possible combination therapies for first-line treatment of pancreatic cancer, and Tarceva, under development by OSI Pharmaceuticals, Genentech and Roche, is being evaluated as a single-agent therapy for the first-line treatment of pancreatic cancer. Orathecin[™] from SuperGen is under NDA review by the FDA for second-line treatment of pancreatic cancer. PANVAC-VF, a vaccine under development by Therion Biologics, is also entering Phase 3 trials as a second line treatment for pancreatic cancer.

Competition for our BPH Product Candidate

Our TH-070 product candidate for the treatment of symptomatic BPH will compete with alpha adrenergic receptor blockers, including Flomax[®], co-marketed by Boehringer Ingelheim and Abbott Laboratories, and Cardura[®], marketed by Pfizer, and with 5-alpha reductase inhibitors, including Proscar[®], marketed by Merck, Avodart[®], marketed by GlaxoSmithKline, and Xatral[®], marketed by the sanofi-aventis Group. In addition, we are aware that other companies are developing drugs for the treatment of BPH. We also will compete with other treatment alternatives such as surgery and other non-drug interventions. The leading BPH drugs are Flomax, which had worldwide 2003 sales of approximately \$1 billion, and Proscar, which had worldwide 2003 sales of approximately \$600 million. Alpha adrenergic receptor blockers, such as Flomax, work by relaxing the smooth muscle in the urethra and bladder and do not address the underlying condition of the enlarged prostate. 5-alpha reductase inhibitors, such as Proscar, work by blocking production of the hormones that stimulate the growth of new prostate cells but do not immediately kill existing cells. Consequently, this class of drugs has a slow onset, typically requiring daily treatment for many months before improving patient symptoms. Drugs in both classes can have significant side effects, including decreased libido, impotence and cardiovascular effects. Many patients ultimately fail existing medical therapy, leading to 350,000 surgical procedures annually in the United States, despite the risks of serious surgical complications including impotence and incontinence.

Governmental Regulation and Product Approval

The manufacturing and marketing of our potential products and our ongoing research and development activities are subject to extensive regulation by the FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries.

United States Regulation

Before any of our products can be marketed in the United States, they must secure approval by the FDA. To secure this approval, any drug we develop must undergo rigorous preclinical testing and clinical trials that demonstrate the product candidate's safety and effectiveness for each chosen indication for use. This extensive regulatory process controls, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale, and distribution of biopharmaceutical products.

In general, the process required by the FDA before investigational drugs may be marketed in the United States involves the following steps:

- pre-clinical laboratory and animal tests;
- submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use;

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- pre-approval inspection of manufacturing facilities and selected clinical investigators; and
- FDA approval of a new drug application, or NDA, or of a NDA supplement (for subsequent indications).

Preclinical Testing

In the United States, drug candidates are tested in animals until adequate proof of safety is established. These preclinical studies generally evaluate the mechanism of action of the product and assess the potential safety and efficacy of the product. Tested compounds must be produced according to applicable current good manufacturing practice (cGMP) requirements and preclinical safety tests must be conducted in compliance with FDA and international regulations regarding good laboratory practices (GLP). The results of the preclinical tests, together with manufacturing information and analytical data, are generally submitted to the FDA as part of an investigational new drug application, or IND, which must become effective before human clinical trials may commence. The IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA requests an extension or raises concerns about the conduct of the clinical trials as outlined in the application. If the FDA has any concerns, the sponsor of the application and the FDA must resolve the concerns before clinical trials can begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, and the FDA must grant permission for each clinical trial to start and continue. Regulatory authorities may require additional data before allowing the clinical studies to commence or proceed from one Phase to another, and could demand that the studies be discontinued or suspended at any time if there are significant safety issues. Furthermore, an independent institutional review board (IRB) for each medical center proposing to participate in the conduct of the clinical trial must review and approve the clinical protocol and patient informed consent before the center commences the study.

Clinical Trials

Clinical trials for new drug candidates are typically conducted in three sequential phases that may overlap. In Phase 1, the initial introduction of the drug candidate into human volunteers, the emphasis is on testing for safety or adverse effects, dosage, tolerance, metabolism, distribution, excretion, and clinical pharmacology. Phase 2 involves studies in a limited patient population to determine the initial efficacy of the drug candidate for specific targeted indications, to determine dosage tolerance and optimal dosage and to identify possible adverse side effects and safety risks. Once a compound shows evidence of effectiveness and is found to have an acceptable safety profile in Phase 2 evaluations, pivotal Phase 3 trials are undertaken to more fully evaluate clinical outcomes and to establish the overall risk/benefit profile of the drug, and to provide, if appropriate, an adequate basis for product labeling. During all clinical trials, physicians will monitor patients to determine effectiveness of the drug candidate and to observe and report any reactions or safety risks that may result from use of the drug candidate. The FDA, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk.

The data from the clinical trials, together with preclinical data and other supporting information that establishes a drug candidate's safety, are submitted to the FDA in the form of a new drug application, or NDA, or NDA supplement (for approval of a new indication if the product candidate is already approved for another indication). Under applicable laws and FDA regulations, each NDA submitted for FDA approval is usually given an internal administrative review within 45 to 60 days following submission of the NDA. If deemed complete, the FDA will "file" the NDA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal substantive review goals of six months for priority NDAs (for drugs addressing serious or life threatening conditions for which there is an unmet medical need) and ten months for regular NDAs. The FDA, however, is not legally required to complete its review within these periods, and these performance goals may change over time. Moreover, the outcome of the review, even if generally favorable, is not typically an actual approval, but an "action letter" that describes additional work that must be done before the NDA can be approved. The FDA's

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review of a NDA may involve review and recommendations by an independent FDA advisory committee. The FDA may deny approval of a NDA or NDA supplement if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or an additional pivotal Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval.

Data Review and Approval

Satisfaction of FDA requirements or similar requirements of state, local, and foreign regulatory agencies typically takes several years and requires the expenditure of substantial financial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit, or prevent regulatory approval at any stage of the process. Accordingly, the actual time and expense required to bring a product to market may vary substantially. We cannot assure you that we will submit applications for required authorizations to manufacture and/or market potential products or that any such application will be reviewed and approved by the appropriate regulatory authorities in a timely manner, if at all. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit, or prevent regulatory approval. Success in early stage clinical trials does not ensure success in later stage clinical trials. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations, and dosages, or have conditions placed on them that restrict the commercial applications, advertising, promotion, or distribution of these products.

Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. The FDA may also request additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after a drug receives approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA's voluntary adverse drug reaction reporting system. Any products manufactured or distributed by us pursuant to FDA approvals would be subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with good manufacturing practices, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the good manufacturing practices regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug. Furthermore, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

The FDA closely regulates the marketing and promotion of drugs. Approval may be subject to post-marketing surveillance and other record keeping and reporting obligations, and involve ongoing requirements. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' communications on the subject of off-label use.

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Fast Track Approval

The Federal Food, Drug and Cosmetic Act, as amended, and FDA regulations provide certain mechanisms for the accelerated “Fast Track” approval of potential products intended to treat serious or life-threatening illnesses that have been studied for safety and effectiveness and that demonstrate the potential to address unmet medical needs. The procedures permit early consultation and commitment from the FDA regarding the preclinical and clinical studies necessary to gain marketing approval. Provisions of this regulatory framework also permit, in certain cases, NDAs to be approved on the basis of valid indirect measurements of benefit of product effectiveness, thus accelerating the normal approval process. Certain potential products employing our technology might qualify for this accelerated regulatory procedure. Even if the FDA agrees that these potential products qualify for accelerated approval procedures, the FDA may deny approval of our drugs or may require additional studies before approval. The FDA may also require us to perform post-approval, or Phase 4, studies as a condition of such early approval. In addition, the FDA may impose restrictions on distribution and/or promotion in connection with any accelerated approval, and may withdraw approval if post-approval studies do not confirm the intended clinical benefit or safety of the potential product.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting a NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. If a product that has orphan drug designation subsequently receives FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease, except in very limited circumstances, for seven years. These circumstances are an inability to supply the drug in sufficient quantities or a situation in which a new formulation of the drug has shown superior safety or efficacy. This exclusivity, however, also could block the approval of our product for seven years if a competitor obtains earlier approval of the same drug for the same indication.

We intend to file for orphan drug designation for all of our oncology product candidates. Obtaining FDA approval to market a product with orphan drug exclusivity may not provide us with a material commercial advantage.

Drug Price Competition and Patent Term Restoration Act of 1984

Under the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Amendments, a portion of a product’s patent term that was lost during clinical development and application review by the FDA may be restored. The Hatch-Waxman Amendments also provide for a statutory protection, known as nonpatent market exclusivity, against the FDA’s acceptance or approval of certain competitor applications. The Hatch-Waxman Amendments also provide the legal basis for the approval of abbreviated new drug applications (ANDAs, for generic drugs).

Patent term restoration can compensate for time lost during product development and the regulatory review process by returning up to five years of patent life for a patent that covers a new product or its use. This period is generally one-half the time between the effective date of an IND (falling after issuance of the patent) and the submission date of a NDA, plus the time between the submission date of a NDA and the approval of that application. Patent term restorations, however, are subject to a maximum extension of five years, and the patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years. The application for patent term extension is subject to approval by the United States Patent and Trademark Office in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension. Up to five years of interim one year extensions are available if a product is still undergoing development or FDA review at the time of its expiration.

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The Hatch-Waxman Amendments also provide for a period of statutory protection for new drugs that receive NDA approval from the FDA. If a new drug receives NDA approval as a new chemical entity, meaning that the FDA has not previously approved any other new drug containing the same active moiety, then the Hatch-Waxman Amendments prohibit an abbreviated new drug application or a NDA where the applicant does not own or have a legal right of reference to all of the data required for approval (a “505(b)(2)” NDA) to be submitted by another company for a generic version of such drug, with some exceptions, for a period of five years from the date of approval of the NDA. The statutory protection provided pursuant to the Hatch-Waxman Amendments will not prevent the filing or approval of a full NDA. In order to gain approval of a full NDA, however, a competitor would be required to conduct its own preclinical investigations and clinical trials. If NDA approval is received for a new drug containing an active ingredient that was previously approved by the FDA but the NDA is for a drug that includes an innovation over the previously approved drug, for example, a NDA approval for a new indication or formulation of the drug with the same active ingredient, and if such NDA approval was dependent upon the submission to the FDA of new clinical investigations, other than bioavailability studies, then the Hatch-Waxman Amendments prohibit the FDA from making effective the approval of an ANDA or a 505(b)(2) NDA for a generic version of such drug for a period of three years from the date of the NDA approval. This three year exclusivity, however, only covers the innovation associated with the NDA to which it attaches. Thus, the three year exclusivity does not prohibit the FDA, with limited exceptions, from approving ANDAs or 505(b)(2) NDAs for drugs containing the same active ingredient but without the new innovation.

While the Hatch-Waxman Amendments provide certain patent term restoration and exclusivity protections to innovator drug manufacturers, it also permits the FDA to approve ANDAs for generic versions of their drugs. The ANDA process permits competitor companies to obtain marketing approval for a drug with the same active ingredient for the same uses but does not require the conduct and submission of clinical studies demonstrating safety and effectiveness for that product. Instead of safety and effectiveness data, an ANDA applicant needs only to submit data demonstrating that its product is bioequivalent to the innovator product as well as relevant chemistry, manufacturing and product data. The Hatch-Waxman Amendments also instituted a third type of drug application that requires the same information as a NDA including full reports of clinical and preclinical studies except that some of the information from the reports required for marketing approval comes from studies which the applicant does not own or have a legal right of reference. This type of application (a “505(b)(2) NDA”) permits a manufacturer to obtain marketing approval for a drug without needing to conduct or obtain a right of reference for all of the required studies.

Finally, the Hatch-Waxman Amendments require, in some circumstances, an ANDA or a 505(b)(2) NDA applicant to notify the patent owner and the holder of the approved NDA of the factual and legal basis of the applicant’s opinion that the patent listed by the holder of the approved NDA in FDA’s Orange Book is not valid or will not be infringed (the patent certification process). Upon receipt of this notice, the patent owner and the NDA holder have 45 days to bring a patent infringement suit in federal district court and obtain a 30-month stay against the company seeking to reference the NDA. The NDA holder could still file a patent suit after the 45 days, but if they did, they would not have the benefit of the 30-month stay. Alternatively, after this 45-day period, the applicant may file a declaratory judgment action, seeking a determination that the patent is invalid or will not be infringed. Depending on the circumstances, however, the applicant may not be able to demonstrate a controversy sufficient to confer jurisdiction on the court. The discovery, trial and appeals process in such suits can take several years. If such a suit is commenced, the Hatch-Waxman Act provides a 30-month stay on the approval of the competitor’s ANDA or 505(b)(2) NDA. If the litigation is resolved in favor of the competitor or the challenged patent expires during the 30-month period, unless otherwise extended by court order, the stay is lifted and the FDA may approve the application. Under regulations recently issued by the FDA, and essentially codified under the recent Medicare prescription drug legislation, the patent owner and the NDA holder have the opportunity to trigger only a single 30-month stay per ANDA or 505(b)(2) NDA. Once the ANDA or 505(b)(2) NDA applicant has notified the patent owner and the NDA holder of the infringement, the applicant cannot be subjected to another 30-month stay, even if the applicant becomes aware of additional patents that may be infringed by its product.

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Foreign Approvals

In addition to regulations in the United States, we will be subject to a variety of foreign regulations 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 foreign countries 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.

Under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

The policies of the FDA and foreign regulatory authorities may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our investigational drugs or approval of new diseases for our existing products. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

Other Government Regulation

Our research and development activities use biological and hazardous materials that are dangerous to human health and safety or the environment. We are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these materials and wastes resulting from these materials. We are also subject to regulation by the Occupational Safety and Health Administration, or OSHA, the California and federal environmental protection agencies and to regulation under the Toxic Substances Control Act. OSHA or the California or federal EPA may adopt regulations that may affect our research and development programs. We are unable to predict whether any agency will adopt any regulations that could have a material adverse effect on our operations. We have incurred, and will continue to incur, capital and operating expenditures and other costs in the ordinary course of our business in complying with these laws and regulations.

Legal Proceedings

We are not currently involved in any material legal proceedings.

Facilities

We sublease approximately 33,700 square feet of laboratory and office space in Redwood City, California, under an agreement that terminates in February 2010.

Employees

As of November 30, 2004 we had 42 employees, including 11 who hold Ph.D. and/or M.D. degrees. 25 of our employees are engaged in research and development, and our remaining employees are management or administrative staff. None of our employees is subject to a collective bargaining agreement. We believe that we have good relations with our employees.

MANAGEMENT

Officers and Directors

The following table sets forth, as of November 30, 2004, information about our executive officers and directors.

Name	Age	Position(s)
<i>Executive Officers and Directors</i>		
Harold E. Selick, Ph.D.	50	Chief Executive Officer and Director
George F. Tidmarsh, M.D., Ph.D.	44	Founder, President and Director
Janet I. Swearson	56	Chief Financial Officer, Vice President Finance and Operations
Wilfred E. Jaeger, M.D. ⁽¹⁾⁽²⁾	48	Director
Michael F. Powell, Ph.D. ⁽¹⁾⁽²⁾	50	Director
Ralph E. Christoffersen, Ph.D. ⁽²⁾⁽³⁾	66	Director
Patrick G. Enright ⁽¹⁾⁽³⁾	42	Director
William A. Halter ⁽³⁾	44	Director
George G.C. Parker, Ph.D.	65	Director
<i>Significant Employee</i>		
Mark G. Matteucci, Ph.D.	50	Vice President of Discovery

- (1) Member of the audit committee
- (2) Member of the compensation committee
- (3) Member of the nominating and governance committee

Harold E. Selick, Ph.D. joined us as Chief Executive Officer in May 2003. Since June 2002, Dr. Selick has been a Venture Partner of Sofinnova Ventures, Inc., a venture capital firm. From January 1999 to April 2002, he was Chief Executive Officer of Camitro Corporation, a biotechnology company. From 1992 to 1999, he was at Affymax Research Institute, the drug discovery technology development center for Glaxo Wellcome plc, most recently as Vice President of Research. Prior to working at Affymax he held scientific positions at Protein Design Labs, Inc. and Anergen, Inc. Dr. Selick received his B.S. and Ph.D. from the University of Pennsylvania and was a Damon Runyon-Walter Winchell Cancer Fund Fellow and an American Cancer Society Senior Fellow at the University of California, San Francisco.

George F. Tidmarsh, M.D., Ph.D. is our founder and has served as a member of our board of directors and as our President since October 2001. From April 2001 to September 2001, Dr. Tidmarsh was an entrepreneur-in-residence at Three Arch Partners, the venture capital firm that provided initial financing to the company. From October 1996 to December 2000, he held various positions at Coulter Pharmaceuticals, Inc., including chief medical officer from September 1998. Prior to that he held scientific and clinical positions at SEQUUS, Gilead Sciences and SyStemix, Inc. He received his M.D. and Ph.D. from the Stanford University School of Medicine where he also completed fellowships in Pediatric Oncology and Neonatal Intensive Care. In addition, he has been a clinical staff member at Stanford Children's Hospital and El Camino Hospital.

Janet I. Swearson has served as our Chief Financial Officer and Vice President, Finance and Operations since September 2002. From 1999 to 2001, Ms. Swearson was Chief Financial Officer and Vice President, Finance and Operations of Camitro Corporation, a biotechnology company. From 1997 to 1999, she was Chief Financial Officer and Vice President, Finance and Administration of IntraBiotics Pharmaceuticals, Inc., a biotechnology company. From 1991 to 1997, Ms. Swearson served in a variety of positions at Affymax Research Institute, including Vice President, Finance and Operations, Senior Director, Director and Controller. She received her B.A. from the University of Minnesota, Duluth and her M.B.A. from Santa Clara University.

Wilfred E. Jaeger, M.D. has served as a member of our board of directors since 2001. He has been a Partner of Three Arch Partners, a venture capital firm, since 1993. Dr. Jaeger serves as a director of a number of private

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companies. He received his B.S. from the University of British Columbia, his M.D. from the University of British Columbia School of Medicine and his M.B.A. from Stanford University.

Michael F. Powell, Ph.D. has served as a member of our board of directors since 2001. He has been a Managing Director of Sofinnova Ventures, Inc., a venture capital firm, since 1997. Dr. Powell was Group Leader of Drug Delivery at Genentech, Inc. from 1990 to 1997. From 1987 to 1990, he was the Director of Product Development for Cytel Corporation, a biotechnology firm. He was recently an Adjunct Professor at the University of Kansas and an editorial board member of several pharmaceutical journals. Dr. Powell also serves on the board of directors of Seattle Genetics, Inc. and a number of private companies. He received his B.S. and Ph.D. from the University of Toronto and completed his post-doctorate work at the University of California.

Ralph E. Christoffersen, Ph.D. has served as a member of our board of directors since 2003. He has been a Partner of Morgenthaler Management Partners VII, LLC, a private equity firm, since 2001. From 2001 to 2002, he was Chairman of the Board of Ribozyme Pharmaceuticals, Inc., a company involved in developing ribozyme-based therapeutic agents, and from 1992 to 2001, he was Chief Executive Officer and President of Ribozyme Pharmaceuticals. Prior to joining Ribozyme Pharmaceuticals, he was the Senior Vice President of Research at SmithKline Beecham Corporation, Vice President of Discovery Research at The Upjohn Company and President of Colorado State University. Dr. Christoffersen also serves as a director of Serologicals Corp. and a number of private companies. He received his B.S. from Cornell College and his Ph.D. from Indiana University and did his post-doctorate work at Nottingham University, United Kingdom and Iowa State University. He also holds an honorary doctor of law degree from Cornell College.

Patrick G. Enright has served as a member of our board of directors since 2003. He has been a Principal of Pequot Capital Management, Inc., an investment management firm, and a General Partner of Pequot's venture capital and private equity funds since June 2002. From 1998 to 2001, Mr. Enright was a Managing Member of Diaz & Atschul Group, LLC, a principal investment group. From 1995 to 1998, he served in various executive positions at Valentis, Inc., including Senior Vice President, Corporate Development and Chief Financial Officer. From 1993 to 1994, he was Senior Vice President of Finance and Business Development for Boehringer Mannheim Therapeutics, a pharmaceutical company and a subsidiary of Corange Ltd. From 1989 to 1993, Mr. Enright was employed at PaineWebber Incorporated, an investment banking firm, where he became a Vice President in 1992. Mr. Enright is also currently a director of Valentis, Inc. and a number of private companies. Mr. Enright received his B.S. from Stanford University and his M.B.A. from the Wharton School of Business at the University of Pennsylvania.

William A. Halter has served as a member of our board of directors since October 2004. Mr. Halter was Acting Commissioner and Deputy Commissioner of the Social Security Administration from 1999 to 2001. From 1993 to 1999, Mr. Halter served as Senior Advisor of the Office of Management and Budget in the Executive Office of the President of the United States. Mr. Halter also served as Economist for the Joint Economic Committee of Congress and as Chief Economist for the U.S. Senate Committee on Finance. Prior to entering public service, he was an Associate at McKinsey and Company. Mr. Halter is a Trustee Emeritus of Stanford University where he chaired the Academic Policy Committee and serves on the Humanities and Sciences Council and Stanford Medical School's National Advisory Council. Mr. Halter also serves on the Board of Directors of Akamai Technologies, Inc., Intermune, Inc., webMethods, Inc. and Xenogen, Inc. Mr. Halter received his B.A. from Stanford University and his M.Phil. in Economics from Oxford University where he was a Rhodes Scholar.

George G.C. Parker, Ph.D. has served as a member of our board of directors since October 2004. Dr. Parker is the Dean Witter Distinguished Professor of Finance and Management and previously Senior Associate Dean for Academic Affairs and Director of the MBA Program, Graduate School of Business, Stanford University. He serves as a director of Continental Airlines, Inc., Affinity Group International, Inc., BGI Mutual Funds, Tejon Ranch Company, Converium Holding AG and First Republic Bank. Dr. Parker received his B.A. from Haverford College and his M.B.A. and Ph.D. from Stanford University.

Mark G. Matteucci, Ph.D. joined us as Vice President of Discovery in August 2003. From 1999 to 2002, he provided medicinal chemistry consultation to several biotechnology companies. From 1988 to 1999, he was the

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Director of Bioorganic Chemistry at Gilead Sciences, Inc. where he was the first scientist hired and established that company's research program in nucleic acid targeting. Prior to joining Gilead Sciences. Dr. Matteucci was a scientist at Genentech, Inc. Dr. Matteucci received his B.S. from the Massachusetts Institute of Technology and Ph.D. from the University of Colorado.

Scientific and Clinical Advisors

The following persons are scientific and clinical advisors to the company:

Member	Affiliation	Specialty
James Abbruzzese, M.D.	MD Anderson Cancer Center	Oncology
Michael Brawer, M.D.	Northwest Prostate Institute	Urology
Stephen Carter, M.D.	Former Head of Worldwide Clinical Development, Bristol-Myers Squibb	Oncology
Stuart Holden, M.D.	Warschaw Prostate Cancer Center, Cedars Sinai Medical Center	Urology
Theodore J. Lampidis, Ph.D.	University of Miami	Tumor Cell Metabolism
Bernard Landau, M.D.	Case Western Reserve University	Metabolism and Biochemistry
Marc Lippman, M.D.	University of Michigan	Oncology
Claus G. Roehrborn, M.D.	University of Texas	Urology
Brian Seed, Ph.D.	Harvard University	Molecular Biology
Jonathan W. Simons, M.D.	Emory University	Hematology and Oncology
Alan Venook, M.D.	University of California, San Francisco	Oncology
Richard Wahl, M.D.	The Johns Hopkins University	Nuclear Medicine, Radiology and Positron Emission Tomography Nuclear Medicine

Board of Directors

We currently have eight directors. In accordance with the terms of our amended and restated certificate of incorporation, the terms of office of the directors are divided into three classes:

- the class I directors are Dr. Michael F. Powell and Dr. Ralph E. Christoffersen; their term will expire at the annual meeting of stockholders to be held in 2005.
- the class II directors are Dr. Wilfred E. Jaeger, Dr. George F. Tidmarsh and Mr. Patrick G. Enright; their term will expire at the annual meeting of stockholders to be held in 2006.
- the class III directors are Mr. William A. Halter, Dr. George G.C. Parker and Dr. Harold E. Selick; their term will expire at the annual meeting of stockholders to be held in 2007.

At each annual meeting of stockholders, or special meeting in lieu thereof, after the initial classification of the board of directors, the successors to directors whose terms will then expire will be elected to serve from the time of election and qualification until the third annual meeting following election or special meeting held in lieu thereof. The authorized number of directors may be changed only by resolution adopted by a majority of the board of directors. This classification of the board of directors may have the effect of delaying or preventing changes in control or management.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and governance committee.

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Audit Committee

Our audit committee consists of Mr. Patrick G. Enright (chair), Dr. Wilfred E. Jaeger and Dr. Michael F. Powell. Our audit committee oversees our corporate accounting and financial reporting process. Our audit committee appoints our independent auditor and oversees and evaluates their work, ensures written disclosures and communicates with the independent auditor, meets with management and the independent auditor to discuss our financial statements, meets with the independent auditor to discuss matters that may affect our financial statements and approves all related party transactions. Mr. Enright will be our audit committee financial expert under the SEC rules implementing Section 407 of the Sarbanes-Oxley Act of 2002. We believe that the composition of our audit committee meets the requirements for independence under the current requirements of the Sarbanes-Oxley Act of 2002, the NASDAQ National Market and SEC rules and regulations. We believe that the functioning of our audit committee complies with the applicable requirements of the Sarbanes-Oxley Act of 2002, the NASDAQ National Market and SEC rules and regulations. We intend to comply with future requirements to the extent they become applicable to us.

Compensation Committee

Our compensation committee consists of Dr. Ralph E. Christoffersen (chair), Dr. Wilfred E. Jaeger and Dr. Michael F. Powell. Our compensation committee will develop and review compensation policies and practices applicable to executive officers, review and recommend goals for our Chief Executive Officer and evaluate his performance in light of these goals, review and evaluate goals and objectives for other officers, oversee and evaluate our equity incentive plans and review and approve the creation or amendment of our equity incentive plans. We believe that the composition of our compensation committee meets the requirements for independence under, and the functioning of our compensation committee complies with, any applicable requirements of the Sarbanes-Oxley Act of 2002, the NASDAQ National Market and SEC rules and regulations. We intend to comply with future requirements to the extent they become applicable to us.

Nominating and Governance Committee

Our nominating and governance committee consists of Mr. William A. Halter, (chair), Mr. Patrick G. Enright and Dr. Ralph E. Christoffersen. The committee will recommend nominees to the board of directors. Procedures for the consideration of director nominees recommended by stockholders are set forth in our amended and restated bylaws, which will be effective upon completion of this offering.

Director Compensation

Mr. William A. Halter and Dr. George G.C. Parker each receive \$20,000 as an annual retainer, \$2,500 for any in-person board meeting attended in excess of five in-person meetings per year, \$500 for any telephonic board meeting attended, \$1,000 per year for service on a board committee, if any, and \$2,500 for service as a committee chairperson, if any. We have not provided cash compensation to our other non-employee directors for their services as directors. All of our directors are entitled to reimbursement for all reasonable out-of-pocket expenses incurred in connection with attendance at board and committee meetings.

Following the completion of this offering, all non-employee directors may receive automatic options grants under the 2004 Equity Incentive Plan as more fully described in the section entitled "Employee Benefit Plans—2004 Equity Incentive Plan." All employee directors who are not 5% owners of the company will be eligible to participate in our 2004 Employee Stock Purchase Plan, as more fully described in the section entitled "Employee Benefit Plans—2004 Employee Stock Purchase Plan."

Compensation Committee Interlocks and Insider Participation

Prior to establishing the compensation committee, the board of directors as a whole made decisions relating to compensation of our executive officers. No member of the board of directors or the compensation committee serves as a member of the board of directors or compensation committee of any other entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

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Limitation of Liability and Indemnification of Officers and Directors

Our amended and restated certificate of incorporation limits the liability of directors to the maximum extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except liability for:

- any breach of their duty of loyalty to the corporation or its stockholders;
- acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

Our bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by law, including if he or she is serving as a director, officer, employee or agent of another company at our request. We believe that indemnification under our bylaws covers at least negligence and gross negligence on the part of indemnified parties. Our bylaws also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in connection with their services to us, regardless of whether our bylaws permit such indemnification.

We have entered into separate indemnification agreements with our directors and executive officers, in addition to the indemnification provided for in our bylaws. These agreements, among other things, provide that we will indemnify our directors and executive officers for certain expenses (including attorneys' fees), judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of such person's services as one of our directors or executive officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request. We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and executive officers.

There is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

Executive Compensation

The following table summarizes the compensation paid to, awarded to or earned during the year ended December 31, 2003 by our chief executive officer and our other executive officers who were serving as executive officers on December 31, 2003 and whose salary and bonus exceeded \$100,000 for services rendered to us in all capacities during the year ended December 31, 2003.

Name And Principal Position(s)	Year	Long Term Compensation	
		Annual Compensation Salary	Securities Underlying Options
Harold E. Selick, Ph.D. ⁽¹⁾ <i>Chief Executive Officer</i>	2003	\$ 169,007	764,577
George F. Tidmarsh, M.D., Ph.D. ⁽²⁾ <i>Founder and President</i>	2003	\$ 200,000	—
Janet I. Swearson ⁽³⁾ <i>Chief Financial Officer</i>	2003	\$ 238,500	160,000

- (1) Harold E. Selick, Ph.D., our Chief Executive Officer, initially served as our part-time Acting Chief Executive Officer, in which capacity he earned \$2,340. On May 1, 2003, Dr. Selick converted his position to full-time

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Chief Executive Officer, earning \$166,667 on an annualized salary of \$250,000. As of February 1, 2004, Dr. Selick's annual compensation was increased to \$300,000. In 2004, he received bonuses totalling \$274,614.

- (2) As of February 1, 2004, Dr. Tidmarsh's annual compensation was increased to \$250,000. In 2004, he received bonuses totalling \$236,250.
- (3) Janet I. Swearson, our Chief Financial Officer, initially served as a consultant to the company, in which capacity she earned \$99,750. She commenced her employment in April 2003, earning \$138,750 on an annualized salary of \$185,000. As of February 1, 2004, Ms. Swearson's annual compensation was increased to \$220,000. In 2004, she received bonuses totalling \$91,375.

Option Grants In Year Ended December 31, 2003. The following table sets forth each grant of stock options during the fiscal year ended December 31, 2003 to each of the named executive officers. All options were granted under our 2001 Equity Incentive Plan at an exercise price equal to the fair market value of our common stock, as determined by our board of directors, on the date of grant. The percentage of options granted is based on an aggregate of options to purchase a total of 1,112,577 shares of common stock granted by us during the fiscal year ended December 31, 2003 to our employees. The potential realizable value set forth in the last column of the table is calculated based on the term of the option at the time of grant, which is ten years. This value is based on assumed rates of stock price appreciation of 5% and 10% compounded annually from the date of grant until their expiration date, assuming a fair market value equal to an assumed initial public offering price of \$ (which is the midpoint of the range on the cover of this prospectus), minus the applicable exercise price. These numbers are calculated based on the requirements of the SEC and do not reflect our estimate of future stock price growth. Actual gains, if any, on stock option exercises will depend on the future performance of the common stock on the date on which the options are exercised.

Named Executive Officers	Number of Shares Underlying Options Granted	Percentage of Total Options Granted to Employees	Exercise Price per Share	Expiration Date	Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Term	
					5%	10%
Harold E. Selick, Ph.D. ⁽¹⁾	764,577	68.72%	\$ 0.10	6/23/2013		
George F. Tidmarsh, M.D., Ph.D.	—					
Janet I. Swearson ⁽²⁾	160,000	14.38%	\$ 0.10	6/23/2013		

- (1) Stock options granted to Dr. Selick vested 25% as of the grant date with the remaining shares vesting in equal monthly installments over the following 36 months.
- (2) Stock options granted to Ms. Swearson vest in equal monthly installments over four years from the vesting commencement date.

Aggregated Option Exercises During Year Ended December 31, 2003 And Year-End Option Values. The following table sets forth information for each of the named executive officers regarding the number of shares subject to both exercisable and unexercisable stock options, as well as the value of unexercisable in-the-money options, as of December 31, 2003. There was no public trading market for our common stock as of December 31, 2003. Accordingly, the value of the unexercised in-the-money options at fiscal year-end has been calculated by determining the difference between the exercise price per share and the assumed offering price of \$ per share, which is the midpoint of the range listed on the cover of this prospectus. None of the named executive officers exercised options during the fiscal year ended December 31, 2003.

Named executive officers	Number of Securities Underlying Unexercised Options at December 31, 2003		Value of Unexercised In-The-Money Options at December 31, 2003	
	Exercisable	Unexercisable	Exercisable	Unexercisable
Harold E. Selick, Ph.D.	906,139	—	\$	\$
George F. Tidmarsh, M.D., Ph.D.	882,500	—	\$	\$
Janet I. Swearson	169,750	—	\$	\$

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Change of Control Severance Agreements

In December 2004, we entered into change of control severance agreements with Dr. Selick, Ms. Swearson and Dr. Matteucci. Each of these agreements provides that if such person's employment is terminated by us without cause or is involuntarily terminated, then such person will be entitled to a severance payment consisting of 12 months base salary as in effect as of the date of termination. If such person's employment is terminated without cause or involuntarily terminated within 18 months following a change of control, then such person will be entitled to the following severance benefits: 12 months base salary and any applicable allowances in effect as of the date of termination of, if greater, as in effect in the year in which the change of control occurs, immediate acceleration and vesting of all stock options granted prior to the change of control, the termination of our right to repurchase shares of restricted stock purchased prior to the change of control, extension of the exercise period for stock options granted prior to the change of control to two years following the date of termination and up to 12 months of health benefits.

In December 2004, we entered into a change of control severance agreement with Dr. Tidmarsh that provides that if Dr. Tidmarsh's employment is terminated by us without cause or is involuntarily terminated, then Dr. Tidmarsh will be entitled to a severance payment consisting of 12 months base salary as in effect as of the date of termination. If Dr. Tidmarsh's employment is terminated without cause or involuntarily terminated within 18 months following a change of control, then he will be entitled to the following severance benefits: 12 months base salary and any applicable allowances in effect as of the date of termination or, if greater, as in effect in the year in which the change of control occurs, immediate acceleration and vesting of all stock options granted prior to the change of control, the termination of our right to repurchase shares of restricted stock purchased prior to the change of control, extension of the exercise period for stock options granted prior to the change of control to two years following the date of termination and up to 12 months of health benefits. In addition, in the event Dr. Tidmarsh is no longer an employee but remains a participant on our clinical or scientific advisory board at the time of a change of control and his participation on such board is terminated without cause within 18 months following a change of control, Dr. Tidmarsh will be entitled to the following severance benefits: immediate acceleration and vesting of all stock options granted prior to the change of control, the termination of our right to repurchase shares of restricted stock purchased prior to the change of control and extension of the exercise period for stock options granted prior to the change of control to two years following the date of termination.

Stock Vesting Agreement

In December 2004, we entered into a stock vesting agreement with Dr. Tidmarsh that provides that if either (i) Dr. Tidmarsh remains our full-time employee until December 31, 2005 and Dr. Tidmarsh has satisfactorily completed certain activities or (ii) Dr. Tidmarsh's employment is involuntarily terminated or terminated without cause prior to December 31, 2005, then our right to repurchase up to 356,529 shares of common stock held by Dr. Tidmarsh will terminate, and the vesting of options to purchase up to 200,000 shares of our common stock held by Dr. Tidmarsh will accelerate. In addition, this agreement provides that if Dr. Tidmarsh's employment with us terminates, but he has performed satisfactorily up to the time of termination, he will be given the opportunity to join our clinical or scientific advisory board, and that so long as he remains a member of such board in good standing, our repurchase right with respect to up to 426,563 shares of our common stock will terminate according to the vesting schedule with respect to such shares.

Employee Benefit Plans

2001 Equity Incentive Plan

Our 2001 Equity Incentive Plan, as amended, or the 2001 Plan, was adopted by our board of directors and approved by our stockholders. This plan provides for the grant of shares of stock, incentive stock options and nonstatutory stock options to employees, directors and consultants. Under this plan, we are authorized to grant shares and stock options for the purchase of up to a maximum of 7,000,000 shares of our common stock. Our board of directors has authorized the compensation committee to administer this plan. This plan terminates on December 2, 2011.

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The administrator determines the vesting schedule (if any) applicable to options. The administrator may grant options that are exercisable for unvested shares of common stock and may further specify at the time of grant whether such right of repurchase shall be at either the (i) exercise price paid by the optionee for such shares or (ii) current fair market value, as determined in accordance with the 2001 Plan, upon termination of optionee's employment or other relationship with us. This repurchase right lapses at the same rate as the vesting schedule applicable to the shares underlying the option.

Upon a merger or sale of all or substantially all of our assets or shares of stock, the successor entity may provide for (i) the assumption of the outstanding stock options, (ii) substitution for any outstanding options of new options to purchase shares of the successor entity, or (iii) the accelerated vesting and immediate exercisability of the outstanding options. The acquiring entity may pursue any one or a combination of the actions specified above.

As of September 30, 2004:

- 437,000 shares were issued upon the exercise of options at a purchase price of \$0.32 per share, but were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 423,231 shares were issuable upon exercise of outstanding options granted under this plan at a weighted average exercise price of \$0.24 per share;
- 2,758,923 shares were issued upon exercise of options at a purchase price of \$0.10 per share, 2,320,124 shares were issued upon exercise of options at a purchase price of \$0.16 per share, and 181,500 shares were issued upon exercise of options at a purchase price of \$0.32 per share; and
- 879,222 shares of our common stock remained available for future grants under this plan.

All share numbers reflected in this summary, as well as the exercise price or purchase price applicable to outstanding options or purchase rights, will be automatically proportionately adjusted in the event we make certain changes in our capital structure, such as a stock split, reverse stock split, stock dividend or other similar transaction. Upon the closing of this offering, no additional stock options may be granted under the 2001 Plan, and any unused shares from the 2001 Plan will be included in our 2004 Equity Incentive Plan as described below.

2004 Equity Incentive Plan

In April 2004, our board of directors approved the 2004 Equity Incentive Plan, or 2004 Plan, which will become effective upon the completion of this offering. The 2004 Plan will terminate in 2014 unless it is terminated earlier by our board.

Stock options, stock appreciation rights, or SARs, stock awards and cash awards may be granted under the 2004 Plan. Each is referred to as an award in the 2004 Plan. Options granted under the 2004 Plan may be either "incentive stock options," as defined under Section 422 of the Internal Revenue Code of 1986, as amended, or nonstatutory stock options.

Share Reserve. We have reserved a total of 4,000,000 shares of our common stock, plus the shares described below, for issuance under the 2004 Plan, all of which are available for future grant. Awards generally shall not reduce the share reserve until the earlier of vesting or the delivery of the shares pursuant to an award. Shares reserved under the plan also include (i) shares of common stock available for issuance as of the effective date of this offering under the 2001 Equity Incentive Plan, including the shares subject to outstanding awards under the 2001 Equity Incentive Plan, plus (ii) shares of common stock issued under the 2001 Equity Incentive Plan or the 2004 Plan that are forfeited or repurchased by the Company at or below the original purchase price or that are issuable upon exercise of awards granted pursuant to the 2001 Equity Incentive Plan or the 2004 Plan that expire or become unexercisable for any reason without having been exercised after the effective date of this offering, plus (iii) shares of common stock that are restored by our board or its compensation committee pursuant to provisions in the 2004 Plan that permit options to be settled in shares on a net appreciation basis at our election.

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Automatic Annual Increase of Share Reserve. The 2004 Plan provides that the share reserve will be cumulatively increased on January 1 of each year, beginning January 1, 2005 and for nine years thereafter, by a number of shares that is equal to the lesser of (a) 5% of the number of our company's shares issued and outstanding prior to the preceding December 31, (b) 2,000,000 shares and (c) a number of shares set by our board.

Automatic Grants. The 2004 Plan provides that persons who first become non-employee directors after the effective date of this offering will be automatically granted options under the 2004 Plan in the following amounts: (a) an option to purchase _____ shares of our common stock upon their initial appointment to our board, and (b) commencing in 2005 and provided that such individual has served as a non-employee director for at least six months, an option to purchase _____ shares annually thereafter.

Administration. The 2004 Plan will be administered by the Compensation Committee of our board of directors or a delegated officer in certain instances. The Compensation Committee or officer is referred to in the 2004 Plan as the administrator.

Eligibility. Awards under the 2004 Plan may be granted to our employees, directors and consultants. Incentive stock options may be granted only to our employees. The administrator, in its discretion, approves awards granted under the 2004 Plan.

Termination of Awards. Generally, if an awardee's service to us terminates other than by reason of death, disability, retirement or for cause, vested options and SARs will remain exercisable for a period of three months following the termination of the awardee's service. Unless otherwise provided for by the administrator in the award agreement, if an awardee dies or becomes totally and permanently disabled while an employee or consultant or director, the awardee's vested options and SARs will be exercisable for one year following the awardee's death or disability, or if earlier, the expiration of the term of such award.

Nontransferability of Awards. Unless otherwise determined by the administrator, awards granted under the 2004 Plan are not transferable other than by will, a domestic relations order, or the laws of descent and distribution and may be exercised during the awardee's lifetime only by the awardee.

Stock Options

Exercise Price. The administrator determines the exercise price of options at the time the options are granted. The exercise price of an incentive stock option may not be less than 100% of the fair market value of the our common stock on the date of grant. The exercise price of a nonstatutory stock option may not be less than 85% of the fair market value of our common stock on the date of grant. The fair market value of our common stock will generally be the closing sales price as quoted on the NASDAQ National Market.

Exercise of Option; Form of Consideration. The administrator determines the vesting schedule (if any) applicable to options. The administrator may grant options that are exercisable for unvested shares of common stock. To the extent that an optionee exercises an unvested option, we generally have the right to repurchase any or all of such unvested shares for either the exercise price paid by the optionee for such shares or the lower of the (i) exercise price paid by the optionee for such shares or (ii) current fair market value of such shares, as determined in accordance with the 2004 Plan, upon termination of optionee's employment or other relationship with us. This repurchase right lapses at the same rate as the vesting schedule applicable to the shares underlying the option. The means of payment for shares issued on exercise of an option are specified in each award agreement. The 2004 Plan permits payment to be made by any lawful means including cash, check, wire transfer, other shares of our common stock (with some restrictions), broker-assisted same day sales or cancellation of any debt owed by us or any of our affiliates to the optionholder or in certain instances a delivery of cash or stock for any net appreciation.

Term of Options. The term of an option may be no more than ten years from the date of grant. No option may be exercised after the expiration of its term. Any incentive stock option granted to a ten percent stockholder may not have a term of more than five years.

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Stock Appreciation Rights. The administrator may grant SARs alone, in addition to, or in tandem with, any other awards under this plan. An SAR entitles the participant to receive the amount by which the fair market value of a specified number of shares on the exercise date exceeds an exercise price established by the administrator. The excess amount will be payable in ordinary shares, in cash or in a combination thereof, as determined by the administrator. The terms and conditions of an SAR will be contained in an award agreement. The grant of an SAR may be made contingent upon the achievement of objective performance conditions.

Stock Awards. The administrator may grant stock awards such as bonus stock, restricted stock or restricted stock units. Generally such awards will contain vesting features such that awards will either not be delivered, or may be repurchased by the Company at cost, if the vesting requirements are not met. The administrator will determine the vesting and share delivery terms. In the case of restricted stock units the administrator may in its discretion offer the awardee the right to defer delivery. Stock awards may be settled in cash or stock as determined by the administrator.

2004 Employee Stock Purchase Plan

General. On April 7, 2004, our board adopted the 2004 Employee Stock Purchase Plan (the "Purchase Plan"). The Purchase Plan will become effective on the first day on which price quotations become available for our common stock on the NASDAQ National Market. The Purchase Plan provides our employees with an opportunity to purchase our common stock through accumulated payroll deductions.

Share Reserve. A total of _____ shares of common stock has been reserved for issuance under the Purchase Plan. In addition, the Purchase Plan provides for annual increases in the total number of shares available for issuance under the Purchase Plan on January 1 of each year, by a number of shares that is equal to the least of:

- 1% of the outstanding shares of our common stock on that date;
- _____ shares; or
- a lesser number as determined by the Compensation Committee of our board prior to such January 1.

Administration. The Compensation Committee appointed by our board, administers the Purchase Plan and has full and exclusive authority to interpret the terms of the Purchase Plan and determine eligibility, subject to the limitations of Section 423 of the Code or any successor provision in the Code.

Eligibility. Persons are eligible to participate in the Purchase Plan if they are employed by us or any participating subsidiary for more than 20 hours per week for more than five months in any calendar year. However, no person may participate in the Purchase Plan if, immediately after the grant of the stock purchase rights under the Purchase Plan, such person will own stock possessing five percent or more of the total combined voting power or value of all classes of our capital stock or of any participating subsidiary.

Offering Periods. The Purchase Plan provides for offering periods of 24 months or such shorter period as may be established by the Compensation Committee. The Purchase Plan includes four six-month purchase periods unless otherwise provided by the Compensation Committee. The initial offering and purchase periods commence on the first day on which price quotations for our common stock first become available on the NASDAQ National Market. The initial offering period will end February 14, 2006 and the initial purchase period will end February 14, 2005. Additional offering periods start on either February 15 or August 15 of each year and end on August 14 or February 14 of each year.

Payroll Deductions. The Purchase Plan permits participants to purchase our common stock through payroll deductions of between 1% and 15% of the participant's compensation under the Purchase Plan, up to a maximum of \$21,250 per year, and up to a maximum of 2,500 shares per purchase period. Compensation includes regular salary payments, bonuses, incentive compensation, overtime pay and other compensation as determined from time to time by the board, but excludes all other payments including long-term disability or workers' compensation payments, car allowances, relocation payments and expense reimbursements.

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Purchase Price. Amounts deducted and accumulated for the participant's account are used to purchase shares of our common stock on the last trading day of each purchase period at a price of 85% of the lower of the fair market values of the common stock at the beginning of the offering period and the end of the purchase period without interest. Participants may end their participation at any time during an offering period, and they will be paid their payroll deductions accumulated to that date. Participation ends automatically upon termination of employment and payroll deductions credited to the participant's account are returned to the participant without interest.

Qualification under the Code. The 2004 Purchase Plan is intended to qualify as an "employee stock purchase plan" under Section 423 of the Code.

Nontransferability. Stock purchase rights granted under the Purchase Plan are not transferable by a participant other than by will or the laws of descent and distribution. Shares purchased under the plan can be disposed of upon the provision of a notice.

Change in Control. In the event of a merger or other corporate transaction, the Purchase Plan will continue for the remainder of all open offering periods that commenced prior to the closing of the merger or other corporate transaction and shares will be purchased based on the fair market value of the surviving corporation's stock on each purchase date (taking account of the exchange ratio where necessary) unless otherwise determined by the Compensation Committee. In the event of a dissolution or liquidation of our company, the offering period will terminate immediately prior to the event, unless otherwise determined by the Compensation Committee. In exercising its discretion, the Compensation Committee may terminate the Purchase Plan after notice to participants.

Amendment and Termination. The board has the authority to amend or terminate the Purchase Plan at any time, including amendments to outstanding stock purchase rights under these plan, subject to required approvals of our stockholders in order for the Purchase Plan to qualify under Section 423 of the Code or other applicable law.

401(k) Plan

We have established and maintained a retirement savings plan under section 401(k) of the Code to cover our eligible employees. The Code allows eligible employees to defer a portion of their compensation, within prescribed limits, on a tax deferred basis through contributions to the 401(k) plan. Our 401(k) plan is qualified under Section 401(a) of the Code and its associated trust is exempt from federal income taxation under Section 501(a) of the Code. Our 401(k) permits us to make matching contributions on behalf of eligible employees; however, we currently do not make these matching contributions.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions:

- to which we are a party;
- in which the amount involved exceeds \$60,000; and
- in which any director, executive officer or holder of more than 5% of our capital stock had or will have a direct or indirect material interest.

Preferred Stock Issuances

On October 29, 2001 and February 7, 2002, we sold an aggregate of 7,500,000 shares of Series A preferred stock at a price per share of \$0.10, for an aggregate purchase price of \$0.8 million. On August 15, 2002, we affected a 1:10 reverse stock split of our capital stock and sold an additional 8,250,000 shares (post-stock split) of Series A preferred stock at a price per share of \$1.00, for an aggregate purchase price of \$8.3 million. Following the reverse stock split and the August 15, 2002 sale of additional shares of Series A preferred stock, we had 9,000,000 shares of Series A preferred stock issued and outstanding. On November 17, 2003, we sold an aggregate of 24,848,484 shares of Series B preferred stock at a price per share of \$1.65, for an aggregate purchase price of \$41.0 million. Each share of Series A preferred stock and Series B preferred stock will convert automatically into one share of common stock upon the closing of this offering.

The following holders of more than 5% of our securities purchased securities in our preferred stock financings in the amounts and as of the dates shown below.

Investor	Series A Preferred Stock	Series B Preferred Stock
Entities affiliated with Morgenthaler Management Partners VII, LLC ⁽¹⁾	—	5,454,545
Entities affiliated with Pequot Capital Management, Inc. ⁽²⁾	—	5,454,545
Entities affiliated with ProQuest Investments	2,250,000	3,030,303
Entities affiliated with Sofinnova Ventures, Inc. ⁽³⁾	2,250,000	3,030,303
Entities affiliated with Three Arch Partners ⁽⁴⁾	2,250,000	3,030,303
Entities affiliated with Sutter Hill Ventures	1,589,079	2,140,175
Total	8,339,079	22,140,174

(1) Ralph E. Christoffersen, one of our directors, is a Partner of Morgenthaler Management Partners VII, LLC.

(2) Patrick G. Enright, one of our directors, is a Principal of Pequot Capital Management, Inc. and a General Partner of the Pequot venture capital and private equity funds.

(3) Michael F. Powell, one of our directors, and Harold E. Selick, our Chief Executive Officer and one of our directors, are a Managing Director and Venture Partner, respectively, of Sofinnova Ventures, Inc.

(4) Wilfred E. Jaeger, one of our directors, is a Partner of Three Arch Partners. Additionally, George F. Tidmarsh, our President and one of our directors, served as an entrepreneur-in-residence at Three Arch Partners immediately prior to our inception.

Shares held by all affiliated persons and entities have been aggregated. For additional details on the shares held by each of these purchasers, please refer to the information in this prospectus under the heading “Principal Stockholders.” Each share of preferred stock will convert automatically into common stock upon the closing of this offering. The purchasers of these shares are entitled to certain registration rights. See “Description of Capital Stock—Registration Rights.”

Other Related Party Transactions and Business Relationships

Harold E. Selick has served as a venture partner of Sofinnova Ventures, Inc., a holder of more than 5% of our common stock, since June 2002. In 2003, Dr. Selick received \$152,083.36 in compensation from Sofinnova Ventures, Inc. Dr. Selick also has a carried interest in a company in which Sofinnova Ventures, Inc. is an investor.

On September 9, 2002, we entered into a consulting agreement with Janet I. Swearson, our Chief Financial Officer. Under the agreement, Ms. Swearson agreed to provide us with financial consulting in exchange for \$1,500 a day and a grant of an option to purchase 9,750 shares of our common stock. The agreement was terminated in April 2003 when Ms. Swearson commenced her full-time employment with us as our Chief Financial Officer.

Our amended and restated certificate of incorporation and bylaws provide that we will indemnify each of our directors and officers to the fullest extent permitted by Delaware Law. Further, we have entered into separate indemnification agreements with each of our directors and executive officers. For further information, see “—Limitation of Liability and Indemnification of Officers and Directors.”

In connection with the sale of our Series B preferred stock, we entered into an Amended and Restated Investors Rights Agreement with the purchasers of such stock granting them certain registration rights. For further information, see “Description of Capital Stock.”

In November 2004, we entered into a Development Agreement with MediBIC Co. Ltd. The Chief Operating Officer and a director of Anexus Pharmaceuticals, Inc., a subsidiary of MediBIC, is the wife of our Chief Executive Officer.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding beneficial ownership of our common stock as of September 30, 2004, and as adjusted to reflect the sale of shares of our common stock offered by this prospectus, by:

- each of our directors and the named executive officers;
- all of our directors and executive officers as a group; and
- each person or group of affiliated persons known by us to be the beneficial owner of more than 5% of our common stock.

Beneficial ownership and percentage ownership are determined in accordance with the rules of the SEC and includes voting or investment power with respect to shares of stock. This information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, shares of common stock issuable under stock options that are exercisable within 60 days of September 30, 2004 are deemed outstanding for the purpose of computing the percentage ownership of the person holding the options but are not deemed outstanding for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated and subject to applicable community property laws, to our knowledge, each stockholder named in the following table possesses sole voting and investment power over their shares of common stock, except for those jointly owned with that person's spouse. Percentage of beneficial ownership before the offering is based on 39,396,531 shares of common stock outstanding as of September 30, 2004 assuming the conversion of all of our outstanding convertible preferred stock and shares of common stock immediately outstanding after completion of this offering. Unless otherwise noted below, the address of each person listed on the table is c/o Threshold Pharmaceuticals, Inc., 951 Gateway Boulevard, South San Francisco, CA 94080-7024.

Name And Address Of Beneficial Owner	Number of Shares Beneficially Owned Prior to Offering	Percent Of Shares Beneficially Owned	
		Before Offering	After Offering
Holders of more than 5% of our voting securities			
Entities affiliated with Morgenthaler Partners VII, LLC ⁽¹⁾ 2710 Sand Hill Road Suite 100 Menlo Park, CA 94025	5,454,545		
Pequot Capital Management, Inc. ⁽²⁾ 500 Nyala Farm Road Westport, CT 06880	5,454,545		
Entities affiliated with ProQuest Investments ⁽³⁾ 12626 High Bluff Drive Suite 360 San Diego, California 92130	5,280,303		
Entities affiliated with Sofinnova Ventures, Inc. ⁽⁴⁾ 140 Geary Street Tenth Floor San Francisco, CA 94108	5,280,303		
Entities affiliated with Three Arch Partners ⁽⁵⁾ 3200 Alpine Road Portola Valley, CA 94028	5,280,303		
Entities affiliated with Sutter Hill Ventures ⁽⁶⁾ 755 Page Mill Road, Suite A-200 Palo Alto, CA 94304-1005	3,729,254		

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Name And Address Of Beneficial Owner	Number of Shares Beneficially Owned Prior to Offering	Percent Of Shares Beneficially Owned	
		Before Offering	After Offering
Directors and Named Executive Officers			
Harold E. Selick, Ph.D. ⁽⁷⁾	1,856,139		
George F. Tidmarsh, M.D., Ph.D. ⁽⁸⁾	1,857,500		
Janet I. Swearson ⁽⁹⁾	574,750		
Ralph E. Christoffersen ⁽¹⁰⁾	5,454,545		
Patrick G. Enright ⁽¹¹⁾	5,454,545		
Wilfred E. Jaeger ⁽¹²⁾	5,280,303		
Michael F. Powell ⁽¹³⁾	5,280,303		
William A. Halter ⁽¹⁴⁾	—		
George G.C. Parker ⁽¹⁵⁾	—		
All directors and executive officers as a group (9 persons) ⁽¹⁶⁾	25,758,085		

- (1) Includes 5,454,545 shares held by Morgenthaler Partners VII, LLC (MP VII). Ralph E. Christoffersen, one of our directors, is a Partner of Morgenthaler Management Partners VII, LLC, the managing partner of MP VII. Dr. Christoffersen, a member of our board of directors, shares voting power over the shares with the other members of MMP VII. The natural persons who have voting or investment power over the shares held of record by MP VII are Robert C. Bellas, Jr., Greg E. Blonder, James W. Broderick, Ralph E. Christoffersen, Andrew S. Lanza, Theodore A. Laufik, Paul H. Levine, Gary R. Little, John D. Lutsi, Gary J. Morgenthaler, Robert D. Pavey, G. Gary Shaffer, Peter G. Taft. Dr. Christoffersen disclaims beneficial ownership of the shares held by MP VII except to the extent of his pecuniary interest therein.
- (2) Includes shares which may be deemed to be beneficially owned by Pequot Capital Management, Inc., the investment manager of Pequot Private Equity Fund III, L.P., which may be deemed to be the holder of record of 4,780,631 shares, and Pequot Offshore Private Equity Partners III, L.P., the holder of record of 673,914 shares. Pequot Capital Management, Inc. holds voting and dispositive power for all shares held by Pequot Private Equity Fund III, L.P., and Pequot Offshore Private Equity Partners III, L.P. (collectively, the “Funds”). Patrick G. Enright is a Principal of Pequot Capital Management, Inc. and a General Partner of each of the Funds. Mr. Enright serves as a member of our board of directors and may be deemed to beneficially own the securities held of record by the Funds. Mr. Enright disclaims beneficial ownership of the shares held by the Funds, except to the extent of his pecuniary interest therein.
- (3) Includes 5,067,507 shares held of record ProQuest Investments II, L.P. and 212,796 shares held of record by ProQuest Investments II Advisors Fund, L.P. The natural persons affiliated with ProQuest Investments who have voting or investment power over these shares are Joyce Tsang, Jay Moorin, Alain Schreiber and Pasquale DeAngelis.
- (4) Includes 5,040,990 shares of record held by Sofinnova Venture Partners V, LP, 165,731 shares of record held by Sofinnova Venture Affiliates V, LP, and 73,582 held by Sofinnova Venture Principals V, LP. The natural person affiliated with Sofinnova Ventures, Inc. who has voting or investment power over these shares is Michael F. Powell. Dr. Powell, a member of our board of directors, disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.
- (5) Includes 5,010,946 shares of record held by Three Arch Partners III, L.P. and 269,357 shares of record held by Three Arch Associates III, L.P. Wilfred E. Jaeger, who serves as a member of our board of directors, is a member of Three Arch Management III, L.L.C., which is the general partner for Three Arch Partners III, L.P. and Three Arch Associates III, L.P. Dr. Jaeger disclaims beneficial ownership of shares held by Three Arch Partners III, L.P., Three Arch Associates III, L.P. and Three Arch Management III, L.L.C., except to the extent of his pecuniary interest therein.
- (6) Includes 92,354 shares held by Sutter Hill Entrepreneurs Fund (AI), L.P.; 36,474 shares held by Sutter Hill Entrepreneurs Fund (QP), L.P.; 3,600,426 shares held by Sutter Hill Ventures, a California Limited Partnership, over which a managing director of the general partner of the partnerships mentioned herein, shares voting and investment power with seven other managing directors of the general partner of the

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- partnerships mentioned herein. The natural persons who have voting or investment power over the shares held of record by Sutter Hill Ventures are David L. Anderson, G. Leonard Baker, Jr., William H. Younger, Jr., Tench Coxe, Gregory P. Sands, James C. Gaither, Jeffrey W. Bird, and James N. White.
- (7) Includes 1,127,646 shares which we have the right to repurchase as of the date that is 60 days after September 30, 2004.
 - (8) Includes 804,515 shares which we have the right to repurchase as of the date that is 60 days after September 30, 2004.
 - (9) Includes 430,834 shares which we have the right to repurchase as of the date that is 60 days after September 30, 2004.
 - (10) Includes 5,454,545 shares held of record by Morgenthaler Partners VII, L.P. (MP VII). Dr. Ralph E. Christoffersen, a member of our board of directors and a Managing Member of MP VII, shares voting or investment power over these shares with Robert C. Bellas, Jr., Greg E. Blonder, James W. Broderick, Andrew S. Lanza, Theodore A. Laufik, Paul H. Levine, Gary R. Little, John D. Lutsi, Gary J. Morgenthaler, Robert D. Pavey, G. Gary Shaffer, Peter G. Taft. Dr. Christoffersen disclaims beneficial ownership in these shares, except to the extent of his pecuniary interest.
 - (11) Includes shares which may be deemed to be beneficially owned by Pequot Capital Management, Inc., the investment manager of Pequot Private Equity Fund III, L.P., the holder of record of 4,780,631 shares, and Pequot Offshore Private Equity Partners III, L.P., which may be deemed to be the holder of record of 673,914 shares. Pequot Capital Management, Inc. holds voting and dispositive power for all shares held by Pequot Private Equity Fund III, L.P., and Pequot Offshore Private Equity Partners III, L.P. (collectively, the "Funds"). Patrick G. Enright is a Principal of Pequot Capital Management, Inc. and a General Partners of each of the Funds. Mr. Enright serves as a member of our board of directors and may be deemed to beneficially own the securities held of record by the Funds. Mr. Enright disclaims beneficial ownership of the shares held by the Funds, except to the extent of his pecuniary interest.
 - (12) Includes 5,280,303 shares held of record by Three Arch Partners III, L.P. and Three Arch Associates III, L.P. Wilfred E. Jaeger, who serves as a member of our board of directors, is a member of Three Arch Management III, L.L.C., which is the general partner for Three Arch Partners III, L.P. and Three Arch Associates III, L.P. Dr. Jaeger disclaims beneficial ownership of shares held by Three Arch Partners III, L.P., Three Arch Associates III, L.P. and Three Arch Management III, L.L.C., except to the extent of his pecuniary interest therein.
 - (13) Includes 5,280,303 shares held of record by Sofinnova Venture Partners V, LP, Sofinnova Venture Affiliates V, LP and Sofinnova Venture Principals V, LP. Michael F. Powell, a member of our board of directors and a Managing Member of Sofinnova Venture Partners, has voting or investment power over these shares.
 - (14) In October 2004, we granted options to purchase a total of 60,000 shares to Mr. Halter, which options are exercisable within 60 days of September 30, 2004, of which 40,000 vest at the rate of $\frac{1}{36}$ per month commencing September 22, 2004 and 20,000 vest on the anniversary of Mr. Halter's appointment to our board of directors commencing in 2005.
 - (15) In October 2004, we granted options to purchase a total of 60,000 shares to Dr. Parker, which options are exercisable within 60 days of September 30, 2004, of which 40,000 vest at the rate of $\frac{1}{36}$ per month commencing September 22, 2004 and 20,000 vest on the anniversary of Dr. Parker's appointment to our board of directors commencing in 2005.
 - (16) Total number of shares includes common stock held by entities affiliated with directors and executive officers. See footnotes 1 through 15 above.

DESCRIPTION OF CAPITAL STOCK

The description below of our capital stock and provisions of our amended and restated certificate of incorporation and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will become effective upon closing of this offering. These documents will be filed as exhibits to the registration statement of which this prospectus is a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur upon the closing of this offering.

Our amended and restated certificate of incorporation, which will become effective upon the closing of this offering, authorizes the issuance of up to 150,000,000 shares of common stock, par value \$0.001 per share, and 2,000,000 shares of preferred stock, par value \$0.001 per share. The rights and preferences of the preferred stock may be established from time to time by our board of directors.

- As of September 30, 2004, 5,548,047 shares of common stock, 33,848,484 shares of preferred stock convertible into 33,848,484 shares of common stock upon the completion of this offering and a warrant to purchase 38,000 shares of preferred stock were issued and outstanding. In addition, as of September 30, 2004, 437,000 shares of common stock were outstanding but subject to a call feature, which call feature has since been cancelled.
- As of September 30, 2004, we had 44 common stockholders of record and 48 preferred stockholders of record.
- Immediately after the closing of this offering, we will have approximately _____ shares of common stock outstanding, assuming no exercise of the underwriters' over-allotment option and no exercise of options to acquire _____ additional shares of common stock.

Common Stock

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, except matters that relate only to one or more of the series of preferred stock and each holder does not have cumulative voting rights. Accordingly, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose.

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by the board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Holders of common stock have no preemptive or conversion rights or other subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are, and the shares of common stock offered by us in this offering, when issued and paid for, will be fully paid and nonassessable. The rights, preferences and privileges of the 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 which we may designate in the future.

Preferred Stock

Upon the closing of this offering, our board of directors will be authorized, subject to any limitations prescribed by law, without stockholder approval, to issue up to an aggregate of 2,000,000 shares of preferred

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stock in one or more series and to fix the rights, preferences, privileges and restrictions granted to or imposed upon the preferred stock, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of holders of any preferred stock that may be issued in the future. Issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could have the effect of delaying, deferring or preventing a change in control of us. We have no present plans to issue any shares of preferred stock.

Warrant

On March 27, 2003, in connection with our loan and security agreement with Silicon Valley Bank, we issued to Silicon Valley Bank a warrant to purchase 38,000 shares of our common stock at an exercise price of \$1.00 per share. The warrant expires on the later of March 27, 2013 or seven years after the closing to this public offering.

Options

We intend to file a registration statement under the Securities Act covering _____ shares of common stock reserved for issuance under our 2001 Equity Incentive Plan, 2004 Equity Incentive Plan and 2004 Employee Stock Purchase Plan. That registration statement is expected to become effective upon filing with the SEC. Accordingly, common stock registered under that registration statement will, subject to vesting provisions and limitations as to the volume of shares that may be held by our affiliates under the Rule 144 described above, be available for sale in the open market unless the holder is subject to the 180-day lock-up period.

As of September 30, 2004, options to purchase 423,231 shares of common stock were issued and outstanding at a weighted average exercise price of \$0.24 per share.

Registration Rights

We and the holders of our preferred stock entered into an amended and restated investor rights agreement, dated November 17, 2003. This agreement provides these holders with customary demand and piggyback registration rights with respect to the shares of common stock to be issued upon conversion of their preferred stock.

Pursuant to the terms of our warrant issued to Silicon Valley Bank, Silicon Valley Bank has customary piggyback registration rights with respect to the shares of common stock to be issued upon exercise of its warrant.

Demand Registration

According to the terms of the amended and restated investor rights agreement, holders of 75% of the common stock of the company issued or issuable upon conversion of the outstanding preferred stock of the company (not including common stock sold to the public under Rule 144, pursuant to a registration statement or held by a holder not having rights under the amended and restated investor rights agreement) have the right to require us to register their shares with the SEC for resale to the public. To demand such a registration, holders who hold together an aggregate of at least 75% of the shares held by persons with such registration rights pursuant to that agreement must request a registration statement to register at least a majority of all shares held by persons with such registration rights. We are not required to effect more than two demand registrations. We have currently not effected, or received a request for, any demand registrations. No demands for registration may be made until the later of 180 days following the later of the effective date of the registration statement of which this prospectus is a part and completion of the distribution of this offering.

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Piggyback Registration

If we file a registration statement for a public offering of any of our securities solely for cash, other than a registration statement relating solely to our stock plans, the holders of demand registration rights will have the right to include their shares in the registration statement. The holders of the warrant to purchase preferred stock has piggyback registration rights as well.

Form S-3 Registration

At any time after we become eligible to file a registration statement on Form S-3, the holders of preferred stock having both demand and piggyback registration rights may require us to file a Form S-3 registration statement. We are obligated to file only two Form S-3 registration statement in any twelve-month period. Furthermore, the aggregate offering proceeds of the requested Form S-3 registration, before deducting underwriting discounts and expenses, must be at least \$1,000,000.

These registration rights are subject to certain conditions and limitations, including the right of the underwriters of an offering to limit the number of shares of common stock to be included in the registration. We are generally required to bear the expenses of all registrations, except underwriting discounts and commissions. However, we will not pay for any expenses of any demand or S-3 registration if the request is subsequently withdrawn by the holders who requested such registration unless the withdrawal is based on material adverse information about the company not available at the time of the registration request or the right to demand one registration is forfeited by all holders of the right. The investors rights agreement also contains our commitment to indemnify the holders of registration rights for losses attributable to statements or omissions by us incurred with registrations under the agreement.

Effect of Certain Provisions of our Amended and Restated Certificate of Incorporation and Bylaws and the Delaware Anti-Takeover Statute

Amended and Restated Certificate of Incorporation and Bylaws

Some provisions of Delaware law and our amended and restated certificate of incorporation and bylaws contain provisions that could make the following transactions more difficult:

- acquisition of us by means of a tender offer;
- acquisition of us by means of a proxy contest or otherwise; or
- removal of our incumbent officers and directors.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids and to promote stability in our management. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

- *Undesignated Preferred Stock.* The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue one or more series of preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.
- *Stockholder Meetings.* Our charter documents provide that a special meeting of stockholders may be called only by the chairman of the board or by our president, or by a resolution adopted by a majority of our board of directors.
- *Requirements for Advance Notification of Stockholder Nominations and Proposals.* Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of

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candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

- *Elimination of Stockholder Action by Written Consent.* Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.
- *Amendment of Bylaws.* Any amendment of our bylaws by our stockholders requires approval by holders of at least 66²/3% of our then outstanding common stock, voting together as a single class.
- *Staggered Board.* Our amended and restated certificate of incorporation provide for the division of our board of directors into three classes, as nearly equal in size as possible, with staggered three-year terms. Under our amended and restated certificate of incorporation and amended and restated bylaws, any vacancy on the board of directors, including a vacancy resulting from an enlargement of the board, may only be filled by vote of a majority of the directors then in office. The classification of the board of directors and the limitations on the removal of directors and filling of vacancies would have the effect of making it more difficult for a third party to acquire control of us, or of discouraging a third party from acquiring control of us.
- *Amendment of Amended and Restated Certificate of Incorporation.* Amendments to certain provisions of our amended and restated certificate of incorporation require approval by holders of at least 66²/3% of our then outstanding common stock, voting together as a single class.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law. This law prohibits a publicly held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned by persons who are directors and also officers and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of our assets involving the interested stockholder;
- in general, any transaction that results in the issuance or transfer by us of any of our stock to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

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Limitation of Liability

Our amended and restated certificate of incorporation provides that no director shall be personally liable to us or to our stockholders for monetary damages for breach of fiduciary duty as a director, except that the limitation shall not eliminate or limit liability to the extent that the elimination or limitation of such liability is not permitted by the Delaware General Corporation Law as the same exists or may hereafter be amended.

The NASDAQ National Market

We have applied to list our common stock on the NASDAQ National Market under the symbol “THLD.”

Transfer Agent and Registrar

Upon the closing of this offering, the transfer agent and registrar for our common stock will be Mellon Investor Services LLC.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and we cannot predict the effect, if any, that market sales of shares or the availability of any shares for sale will have on the market price of the common stock prevailing from time to time. Sales of substantial amounts of our common stock (including shares issued on the exercise of outstanding options and warrants), or the perception that such sales could occur, could adversely affect the market price of our common stock and our ability to raise capital through a future sale of our securities.

Upon completion of this offering, _____ shares of common stock will be outstanding, assuming the issuance of an aggregate of _____ shares of common stock in this offering. The number of shares outstanding after this offering is based on the number of shares outstanding as of September 30, 2004 and assumes no exercise of outstanding options. The _____ shares sold in this offering will be freely tradable without restriction under the Securities Act, unless those shares are purchased by affiliates as that term is defined in Rule 144 under the Securities Act.

The remaining 39,396,531 shares of common stock held by existing stockholders are restricted shares and are subject to the contractual restrictions described below. Restricted shares may be sold in the public market only if registered or if they qualify for an exception from registration under Rules 144 or 701 promulgated under the Securities Act, which are summarized below. All of these restricted shares will be available for resale in the public market in reliance on Rule 144 immediately following this offering and will be subject to lock-up agreements described below.

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 rules are summarized below.

Sales of Restricted Shares and Shares Held by Our Affiliates

In general, under Rule 144 as currently in effect, an affiliate of the Company or a person, or persons whose shares are aggregated, who has beneficially owned restricted securities for at least one year, including the holding period of any prior owner except an affiliate of the Company, would be entitled to sell within any three month period a number of shares that does not exceed the greater of 1% of our then outstanding shares of common stock or the average weekly trading volume of our common stock on the NASDAQ National Market during the four calendar weeks preceding such sale. Sales under Rule 144 are also subject to certain manner of sale provisions, notice requirements and the availability of current public information about the Company. Any person, or persons whose shares are aggregated, who is not deemed to have been an affiliate of the Company at any time during the 90 days preceding a sale, and who has beneficially owned shares for at least two years including any period of ownership of preceding non-affiliated holders, would be entitled to sell such shares under Rule 144(k) without regard to the volume limitations, manner of sale provisions, public information requirements or notice requirements.

Subject to certain limitations on the aggregate offering price of a transaction and other conditions, Rule 701 may be relied upon with respect to the resale of securities originally purchased from the Company by its employees, directors, officers, consultants or advisors prior to the date the issuer becomes subject to the reporting requirements of the Exchange Act. To be eligible for resale under Rule 701, shares must have been issued in connection with written compensatory benefit plans or written contracts relating to the compensation of such persons. In addition, the SEC has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after the date of this offering. Securities issued in reliance on Rule 701 are restricted securities and, subject to the contractual restrictions described above, beginning 90 days after the date of this prospectus, may be sold by persons other than affiliates, subject only to the manner of sale provisions of Rule 144, and by affiliates, under Rule 144 without compliance with its one-year minimum holding period.

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We have reserved an aggregate of 7,000,000 shares of common stock for issuance pursuant to our 2001 Equity Incentive Plan, of which options to purchase approximately 423,321 shares were outstanding as of September 30, 2004. We have also reserved an aggregate of 4,000,000 shares of common stock for issuance under our 2004 Equity Incentive Plan and _____ shares of common stock for issuance under our 2004 Employee Stock Purchase Plan.

As soon as practicable following the offering, we intend to file registration statements under the Securities Act to register shares of common stock reserved for issuance under the 2004 Employee Stock Purchase Plan as well as pre-IPO shares qualified under Rule 701 that may be issued under the 2001 Equity Incentive Plan. Such registration statement will automatically become effective immediately upon filing. Any shares issued upon the exercise of stock options or following purchase under the 2004 Employee Stock Purchase Plan will be eligible for immediate public sale, subject to the lock-up agreements noted below. See “—2004 Employee Stock Purchase Plan” and “—2001 Equity Incentive Plan.”

We have agreed not to sell or otherwise dispose of any shares of common stock during the 180-day period following the date of this prospectus, except we may issue, and grant options to purchase, shares of common stock under the 2004 Employee Stock Purchase Plan and the 2001 Equity Incentive Plan.

Lock-Up Agreements

Each of our executive officers, directors, stockholders and optionholders will have entered into lock-up agreements prior to the commencement of this offering providing, subject to exceptions, that they will not offer to sell, contract to sell or otherwise sell, dispose of, loan, pledge, or grant any rights with respect to any shares of common stock, any options or warrants to purchase, any of the shares of common stock or any securities convertible into, or exercisable or exchangeable for, common stock owned by them, 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, without the prior written consent of Banc of America Securities LLC, for a period of 180 days after the date of this prospectus. The 180-day lock-up period may be extended under certain circumstances where we release, or pre-announce a release of, our earnings or material news or a material event shortly before or after the termination of the 180-day period.

The foregoing does not prohibit open market purchases and sales of our common stock by such holders after the completion of this offering and transfers or dispositions by our officers, directors and stockholders can be made sooner, provided that the transferee agrees to be bound by the 180-day lock-up period:

- as a gift or by will or intestacy;
- to immediate family members; and
- to any trust for the direct or indirect benefit of the holder or his or her immediate family.

Banc of America Securities LLC in its sole discretion and at any time without notice, may release all or any portion of the securities subject to lock-up agreements. When determining whether or not to release shares from the lock-up agreements, Banc of America Securities LLC will consider, among other factors, the stockholder’s reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time. Following the expiration of the 180-day lock-up period, additional shares of common stock will be available for sale in the public market subject to compliance with Rule 144 or Rule 701.

Registration Rights

Upon completion of this offering, the holders of 33,848,484 shares of our common stock, or their transferees, have rights to require or participate in the registration of those shares under the Securities Act. For a detailed description of these registration rights see “Description of Capital Stock—Registration Rights.”

MATERIAL UNITED STATES FEDERAL TAX CONSIDERATIONS FOR NON-UNITED STATES HOLDERS OF OUR COMMON STOCK

The following is a general discussion of the material U.S. federal income and estate tax considerations applicable to non-U.S. holders with respect to their ownership and disposition of shares of our common stock. This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock. In general, a non-U.S. holder means a beneficial owner of our common stock who is not for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the U.S.;
- a corporation, or any other organization taxable as a corporation for U.S. federal tax purposes, created or organized in the U.S. or under the laws of the U.S. or of any state thereof or the District of Columbia; or
- an estate or trust, the income of which is included in gross income for U.S. federal income tax purposes regardless of its source.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, in effect as of the date of this prospectus, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset (generally property held for investment).

This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- partnerships or other pass-through entities;
- regulated investment companies;
- pension plans;
- owners (directly, indirectly or constructively) of more than 5% of our common stock;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- owners that have a functional currency other than the U.S. dollar; and
- certain U.S. expatriates.

There can be no assurance that the Internal Revenue Service, referred to as the IRS, will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, an opinion of counsel or IRS ruling with respect to the U.S. federal income or estate tax consequences to a non-U.S. holder of the purchase, ownership, or disposition of our common stock. **We urge prospective investors to consult with their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of shares of our common stock.**

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Distributions on Our Common Stock

We have not declared or paid distributions on our common stock since our inception and do not intend to pay any distributions on our common stock in the foreseeable future. In the event we do pay distributions on our common stock, however, these distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale, Exchange or Other Disposition of Common Stock."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be provided by an applicable income tax treaty between the U.S. and such holder's country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to withhold any U.S. federal income tax on the distribution as permitted by U.S. Treasury Regulations. If we or another withholding agent withholds tax on such a distribution, a non-U.S. holder may be entitled to a refund of the tax withheld which the non-U.S. holder may claim by filing a U.S. tax return with the IRS.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States (and if an applicable income tax treaty so provides, are also attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder) are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons. Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale, Exchange or Other Disposition of Our Common Stock

In general, a non-U.S. holder will not be subject to any U.S. federal income tax or withholding tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- the gain is effectively connected with a U.S. trade or business (and if an applicable income tax treaty so provides, is also attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder), in which case the graduated U.S. federal income tax rates applicable to U.S. persons and, if the non-U.S. holder is a foreign corporation, the additional branch profits tax described above in "Distributions on Our Common Stock" may apply;
- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax on the net gain derived from the disposition, which may be offset by U.S. source capital losses of the non-U.S. holder, if any; or

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- we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly, indirectly or constructively. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may withhold 10% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons and, if the non-U.S. holder is a foreign corporation, the additional branch profits tax described above in "Distributions on Our Common Stock" may apply. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. Furthermore, no assurance can be provided that our stock will be regularly traded on an established securities market for purposes of the rules described above.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned by an individual non-U.S. holder at the time of death and certain lifetime transfers of an interest in our common stock made by such individual are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person in order to avoid backup withholding with respect to dividends on our common stock. The gross amount of dividends paid to a non-U.S. holder that fails to certify its non-U.S. holder's status in accordance with the applicable U.S. Treasury Regulations generally will be reduced by backup withholding at the applicable rate, currently 28%. Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds where the transaction is effected outside the U.S. through a non-U.S. office of a non-U.S. broker. However, for information reporting purposes, certain brokers with substantial U.S. ownership or operations generally will be treated in a manner similar to U.S. brokers. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

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UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. Banc of America Securities LLC, CIBC World Markets Corp., Lazard Frères & Co. LLC and William Blair & Company, L.L.C are acting as representatives of the underwriters. We have entered into a firm commitment underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

<u>Underwriter</u>	<u>Number of Shares</u>
Banc of America Securities LLC	
CIBC World Markets Corp.	
Lazard Frères & Co. LLC	
William Blair & Company, L.L.C	
Total	

The underwriters initially will offer shares to the public at the price specified on the cover page of this prospectus. The underwriters may allow some dealers a concession of not more than \$ _____ per share. The underwriters also may allow, and any dealers may re-allow, a concession of not more than \$ _____ per share to some other dealers. If all the shares are not sold at the initial public offering price, the underwriters may change the offering price and other selling terms. The common stock is offered subject to a number of conditions, including:

- receipt and acceptance of our common stock by the underwriters, and
- the right to reject orders in whole or in part.

The underwriters have an option to buy up to _____ additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus. The underwriters have 30 days from the date of this prospectus to exercise this option. If the underwriters exercise this option, they will each be obligated, subject to certain conditions, to purchase additional shares approximately in proportion to the amounts specified in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered. We will pay the expenses associated with the exercise of the over-allotment option.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is _____ % of the initial public offering price. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	<u>Paid by Threshold</u>	
	<u>No Exercise</u>	<u>Full Exercise</u>
Per Share	\$ _____	\$ _____
Total	\$ _____	\$ _____

In addition, we estimate that our share of the total expenses of this offering, excluding underwriting discounts and commissions, will be approximately \$ _____.

We and our directors, executive officers, all of our existing stockholders and all of our optionholders will have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant

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to which we and such holders of stock and options have agreed, with limited exceptions, not to sell, directly or indirectly, any shares of our common stock without the prior written consent of Banc of America Securities LLC and CIBC World Markets Corp. for a period of 180 days after the date of this prospectus. This consent may be given at any time without public notice. We have entered into a similar agreement with the representatives of the underwriters, except that we may grant options and sell shares pursuant to our stock plans without such consent. There are no agreements between the representatives and any of our stockholders or affiliates releasing them from these lock-up agreements prior to the expiration of the 180-day period.

We have applied to list our common stock on the NASDAQ National Market under the symbol “THLD.” The underwriters have undertaken to sell and distribute our common stock in compliance with the standards of the NASDAQ National Market.

We will indemnify the underwriters against some specified types of liabilities, including liabilities under the Securities Act of 1933. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress.

These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ over-allotment option referred to above, or may be “naked” shorts, which are short positions in excess of that amount.

The underwriters may close out any covered short position either by exercising their over-allotment option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the over-allotment option.

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 that could adversely affect investors who purchased in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ National Market, in the over-the-counter market or otherwise.

The underwriters do not expect sales to discretionary accounts to exceed _____ % of the total number of shares of common stock offered by this prospectus.

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Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiation between us and the representatives of the underwriters. Among the factors considered in these negotiations are:

- the history of, and prospects for, our company and the industry in which we compete,
- the past and present financial performance of our company,
- an assessment of our management,
- the present state of our development,
- the prospects for our future earnings,
- the prevailing market conditions of the applicable United States securities market at the time of this offering, market valuations of publicly traded companies that we and the representatives of the underwriters believe to be comparable to our company, and
- other factors deemed relevant.

The estimated initial public offering price range set forth on the cover of this preliminary prospectus is subject to change as a result of market conditions and other factors.

We will not offer any shares in this offering on-line or through any other form of prospectus other than a printed prospectus.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Heller Ehrman White & McAuliffe LLP, Menlo Park, CA. Shearman & Sterling LLP, New York, NY is counsel for the underwriters in connection with this offering.

EXPERTS

The financial statements of Threshold Pharmaceuticals, Inc. as of December 31, 2002 and 2003 and for the period from October 17, 2001 (date of inception) to December 31, 2001 and for each of the years ended December 31, 2002 and 2003 included in this prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act of 1933 with respect to the shares of common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement and the exhibits, schedules and amendments to the registration statement. For further information with respect to us and the shares of common stock to be sold in this offering, reference is made to the registration statement. Statements contained in this prospectus as to the contents of any contract, agreement, or other document to which we make reference are not necessarily complete. In each instance, if we have filed a copy of such contract, agreement, or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the matter involved. Each statement regarding a contract, agreement or other document is qualified in all respects by reference to the actual document.

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Upon completion of this offering, we will become subject to the reporting and information requirements of the Securities Exchange Act of 1934 and, as a result, will file periodic and current reports, proxy statements, and other information with the SEC. You may read and copy this information at the Public Reference Room of the SEC located at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. Copies of all or any part of the registration statement may be obtained from the SEC's offices upon payment of fees prescribed by the SEC. The SEC maintains an Internet site that contains periodic and current reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the SEC's website is <http://www.sec.gov>.

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THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Threshold Pharmaceuticals, Inc.

In our opinion, the accompanying balance sheets and the related statements of operations, of stockholders' deficit and of cash flows present fairly, in all material respects, the financial position of Threshold Pharmaceuticals, Inc. (a development stage enterprise) at December 31, 2002 and 2003, and the results of its operations and its cash flows for the period from October 17, 2001 (date of inception) to December 31, 2001 and for the years ended December 31, 2002 and 2003, in conformity with accounting principles generally accepted in the United States of America. 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 of these statements 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, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Jose, California
April 8, 2004

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THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,		September 30, 2004	Pro forma Stockholders' Equity at September 30, 2004
	2002	2003		
				(unaudited)
ASSETS				
Current assets:				
Cash and cash equivalents	\$ 6,215	\$ 40,609	\$ 16,237	
Marketable securities	45	209	12,982	
Prepaid expenses and other current assets	280	128	1,574	
Restricted cash	30	115	85	
	<u>6,570</u>	<u>41,061</u>	<u>30,878</u>	
Total current assets				
Property and equipment, net	71	199	305	
Restricted cash	85	—	192	
Other assets	—	10	—	
	<u>—</u>	<u>10</u>	<u>—</u>	
Total assets	<u>\$ 6,726</u>	<u>\$ 41,270</u>	<u>\$ 31,375</u>	
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)				
Current liabilities:				
Accounts payable	\$ 313	\$ 281	\$ 835	
Accrued liabilities	103	437	1,105	
Notes payable	—	166	211	
Other current liabilities	—	—	140	
	<u>416</u>	<u>884</u>	<u>2,291</u>	
Total current liabilities				
Notes payable, less current portion	—	242	185	
	<u>—</u>	<u>242</u>	<u>185</u>	
Total liabilities	<u>416</u>	<u>1,126</u>	<u>2,476</u>	
Commitments and contingencies (Note 7)				
Redeemable convertible preferred stock, \$0.001 par value:				
Authorized: 33,886,484 shares				
Issued and outstanding: 9,000,000 shares in 2002, 33,848,484 shares in 2003 and 2004 (unaudited) and no shares pro forma (unaudited)				
(Liquidation value: \$49,999,999 at December 31, 2003)	8,977	49,839	49,839	\$ —
	<u>8,977</u>	<u>49,839</u>	<u>49,839</u>	<u>\$ —</u>
Stockholders' equity (deficit):				
Common stock, \$0.001 par value:				
Authorized: 50,000,000 shares				
Issued and outstanding: 291,500 shares in 2002, 304,202 shares in 2003, 5,548,047 shares in 2004 (unaudited) and 39,396,531 shares pro forma (unaudited)				
	—	—	6	39
Additional paid-in-capital	52	2,685	21,900	71,706
Deferred stock-based compensation	(24)	(1,546)	(16,244)	(16,244)
Accumulated other comprehensive income (loss)	(1)	163	98	98
Deficit accumulated during the development stage	(2,694)	(10,997)	(26,700)	(26,700)
	<u>(2,667)</u>	<u>(9,695)</u>	<u>(20,940)</u>	<u>\$ 28,899</u>
Total stockholders' equity (deficit)				
Total liabilities and stockholders' deficit	<u>\$ 6,726</u>	<u>\$ 41,270</u>	<u>\$ 31,375</u>	

The accompanying notes are an integral part of these financial statements.

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THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Period from October 17, 2001 (date of inception) to December 31, 2001	Years Ended December 31,		Nine Months Ended September 30,		Cumulative Period from October 17, 2001 (date of inception) to September 30, 2004
		2002	2003	2003	2004	
				(unaudited)		(unaudited)
Operating expenses:						
Research and development	\$ 35	\$ 2,179	\$ 6,252	\$ 4,868	\$ 10,852	\$ 19,318
General and administrative	201	306	2,057	1,591	5,137	7,701
Total operating expenses	236	2,485	8,309	6,459	15,989	27,019
Loss from operations	(236)	(2,485)	(8,309)	(6,459)	(15,989)	(27,019)
Interest income	—	27	65	17	313	405
Interest expense	—	—	(59)	(24)	(27)	(86)
Net loss	(236)	(2,458)	(8,303)	(6,466)	(15,703)	(26,700)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	(40,862)	—	—	(40,862)
Net loss attributable to common stockholders	\$ (236)	\$(2,458)	\$(49,165)	\$(6,466)	\$(15,703)	\$ (67,562)
Net loss per common share:						
Basic and diluted	\$ (1.29)	\$(21.19)	\$(305.37)	\$(40.92)	\$ (16.14)	
Weighted average number of shares used in per common share calculations:						
Basic and diluted	183	116	161	158	973	
Pro forma net loss per common share (unaudited)(see Note 13):						
Basic and diluted			\$ (4.04)		\$ (0.45)	
Weighted-average number of shares used in pro forma per common share calculations (unaudited)(see Note 13):						
Basic and diluted			12,156		34,821	

The accompanying notes are an integral part of these financial statements.

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THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
STATEMENTS OF STOCKHOLDERS' DEFICIT
FOR THE PERIOD
FROM OCTOBER 17, 2001 (DATE OF INCEPTION) TO SEPTEMBER 30, 2004
(in thousands, except share and per share data)

	Common Stock		Additional Paid-In Capital	Deferred Stock-Based Compensation	Accumulated Other Comprehensive Income (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Deficit
	Shares	Amount					
Issuance of restricted common stock to a founder and member of the Board of Directors in October 2001 for cash at \$0.01 per share	250,000	\$ —	\$ 2	\$ —	\$ —	\$ —	\$ 2
Net loss	—	—	—	—	—	(236)	(236)
Balances, December 31, 2001	250,000	—	2	—	—	(236)	(234)
Issuance of restricted common stock to a member of the Board of Directors for cash at \$0.10 per share in January 2002	37,500	—	4	—	—	—	4
Issuance of common stock pursuant to exercise of stock options for cash at \$0.10 per share	4,000	—	—	—	—	—	—
Deferred stock-based compensation	—	—	25	(25)	—	—	—
Amortization of deferred stock-based compensation	—	—	—	1	—	—	1
Non-employee stock-based compensation	—	—	21	—	—	—	21
Components of other comprehensive income (loss):							
Unrealized loss on marketable securities	—	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	—	(2,458)	(2,458)
Comprehensive loss							(2,459)
Balances, December 31, 2002	291,500	—	52	(24)	(1)	(2,694)	(2,667)
Issuance of common stock pursuant to exercise of stock options for cash at \$0.10 per share	12,702	—	1	—	—	—	1
Issuance of a warrant to purchase Series A redeemable convertible preferred stock	—	—	44	—	—	—	44
Beneficial conversion feature related to issuance of Series B redeemable convertible preferred stock	—	—	40,862	—	—	—	40,862
Deemed dividend related to beneficial conversion feature of Series B redeemable convertible preferred stock	—	—	(40,862)	—	—	—	(40,862)
Deferred stock-based compensation, net of cancellations	—	—	2,332	(2,332)	—	—	—
Amortization of deferred stock-based compensation	—	—	—	810	—	—	810
Non-employee stock-based compensation	—	—	256	—	—	—	256
Components of other comprehensive income (loss):							
Change in unrealized gain (loss) on marketable securities	—	—	—	—	164	—	164
Net loss	—	—	—	—	—	(8,303)	(8,303)
Comprehensive loss							(8,139)
Balances, December 31, 2003	304,202	—	2,685	(1,546)	163	(10,997)	(9,695)
Issuance of common stock pursuant to exercise of stock options for cash at \$0.10 per share (unaudited)	2,742,221	3	271	—	—	—	274
Issuance of common stock pursuant to exercise of stock options for cash at \$0.16 per share (unaudited)	2,320,124	2	369	—	—	—	371
Issuance of common stock pursuant to exercise of stock options for cash at \$0.32 per share (unaudited)	181,500	1	59	—	—	—	60
Deferred stock-based compensation, net of cancellations (unaudited)	—	—	18,120	(18,120)	—	—	—
Amortization of deferred stock-based compensation (unaudited)	—	—	—	3,422	—	—	3,422
Non-employee stock-based compensation (unaudited)	—	—	396	—	—	—	396
Components of other comprehensive income (loss):							
Change in unrealized gain (loss) on marketable securities (unaudited)	—	—	—	—	(65)	—	(65)
Net loss (unaudited)	—	—	—	—	—	(15,703)	(15,703)
Comprehensive loss (unaudited)							(15,768)
Balances, September 30, 2004 (unaudited)	5,548,047	\$ 6	\$ 21,900	\$ (16,244)	\$ 98	\$ (26,700)	\$ (20,940)

The accompanying notes are an integral part of these financial statements.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
STATEMENTS OF CASH FLOWS
(in thousands)

	Period from October 17, 2001 (date of inception) to December 31, 2001	Years Ended December 31,		Nine Months Ended September 31,		Cumulative Period from October 17, 2001 (date of inception) to September 30, 2004
		2002	2003	2003	2004	
				(unaudited)		(unaudited)
Cash flows from operating activities:						
Net loss	\$ (236)	\$ (2,458)	\$ (8,303)	\$ (6,466)	\$ (15,703)	\$ (26,700)
Adjustments to reconcile net loss to net cash used in operating activities:						
Depreciation	—	11	90	65	101	202
Stock-based compensation expense	—	22	1,066	857	3,818	4,906
Amortization of debt issuance costs	—	—	34	30	11	45
Loss on disposal of property and equipment	—	5	—	—	—	5
Changes in operating assets and liabilities:						
Prepays and other current assets	(8)	(272)	152	159	(1,307)	(1,435)
Accounts payable	51	262	(32)	(210)	554	835
Accrued liabilities	142	(39)	334	465	528	965
Net cash used in operating activities	(51)	(2,469)	(6,659)	(5,100)	(11,998)	(21,177)
Cash flows from investing activities:						
Acquisition of property and equipment	—	(87)	(218)	(214)	(206)	(511)
Acquisition of marketable securities	—	(46)	—	—	(19,855)	(19,901)
Proceeds from sale of marketable securities	—	—	—	—	7,017	7,017
Restricted cash	—	(115)	—	—	(162)	(277)
Net cash used in investing activities	—	(248)	(218)	(214)	(13,206)	(13,672)
Cash flows from financing activities:						
Proceeds from redeemable convertible preferred stock, net	236	8,741	40,862	—	—	49,839
Proceeds from issuance of common stock	2	4	1	1	705	712
Proceeds from issuance of unvested options	—	—	—	—	140	140
Proceeds from issuance of notes payable	—	—	510	510	122	632
Repayment of notes payable	—	—	(102)	(62)	(135)	(237)
Net cash provided by financing activities	238	8,745	41,271	449	832	51,086
Net increase (decrease) in cash and cash equivalents	187	6,028	34,394	(4,865)	(24,372)	16,237
Cash and cash equivalents, beginning of period	—	187	6,215	6,215	40,609	—
Cash and cash equivalents, end of period	\$ 187	\$ 6,215	\$ 40,609	\$ 1,350	\$ 16,237	\$ 16,237
Supplemental disclosures:						
Cash paid for interest	\$ —	\$ —	\$ 14	\$ 24	\$ 27	\$ 41
Non-cash financing activities:						
Deferred stock-based compensation	\$ —	\$ 25	\$ 2,332	\$ 2,294	\$ 18,120	\$ 20,477
Fair value of redeemable convertible preferred stock warrant	\$ —	\$ —	\$ 44	\$ 44	\$ —	\$ 44
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	\$ —	\$ —	\$ 40,862	\$ —	\$ —	\$ 40,862

The accompanying notes are an integral part of these financial statements.

**THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS**

NOTE 1—THE COMPANY:

Threshold Pharmaceuticals, Inc. (the “Company”) was incorporated in the State of Delaware on October 17, 2001. The Company is a biotechnology company engaged primarily in the research, development and commercialization of targeted small molecule therapies initially for the treatment of cancer and benign prostatic hyperplasia. The Company is in the development stage and since inception, has devoted substantially all of its time and efforts to performing research and development, raising capital and recruiting personnel.

NOTE 2—SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES:

Unaudited Interim Financial Data

The accompanying balance sheet as of September 30, 2004, the statements of operations and of cash flows for the nine months ended September 30, 2003 and 2004, and the statement of stockholders’ deficit for the nine months ended September 30, 2004 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to state fairly the Company’s financial position and results of operations and cash flows for the nine months ended September 30, 2003 and 2004. The financial data and other information disclosed in these notes to financial statements related to the nine month periods are unaudited. The results for the nine months ended September 30, 2004 are not necessarily indicative of the results to be expected for the year ending December 31, 2004 or for any other interim period or for any future year.

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 disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Cash and cash equivalents

The Company considers all highly liquid investments purchased with original maturities of three months or less to be cash equivalents. All cash and cash equivalents are held in the United States of America in financial institutions and money market funds, which are unrestricted as to withdrawal or use.

Restricted cash

Restricted cash represents two certificates of deposit held at a financial institution. The certificates serve as collateral for the Company’s facility sublease agreements.

Marketable securities

The Company classifies its marketable securities as “available-for-sale.” Such marketable securities are recorded at fair value and unrealized gains and losses are recorded as a separate component of stockholders’ deficit until realized. Realized gains and losses on sale of all such securities will be reported in net loss, computed using the specific identification cost method. The Company places its marketable securities primarily in U.S. government securities, corporate bonds and commercial paper.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

Fair value of financial instruments

Carrying amounts of certain of the Company's financial instruments, including cash and cash equivalents, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities. Based on borrowing rates currently available to the Company for loans with similar terms, the carrying value of the notes payable at December 31, 2003 approximates fair value. Estimated fair values for marketable securities, which are separately disclosed elsewhere, are based on quoted market prices for the same or similar instruments.

Concentration of credit risk and other risks and uncertainties

Financial instruments which potentially subject the Company to concentrations of risk consist principally of cash and cash equivalents. The Company's cash and cash equivalents are invested in deposits with two major banks in the United States of America that management believes are creditworthy. The Company is exposed to credit risk in the event of default by the financial institutions for amounts in excess of Federal Deposit Insurance Corporation insured limits. The Company performs periodic evaluations of the relative credit standings of these financial institutions and limits the amount of credit exposure with any institution.

Any products developed by the Company will require approval from the U.S. Food and Drug Administration ("FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's products will receive the necessary approvals. If the Company is denied such approvals or such approvals are delayed, it could have a material adverse effect on the Company.

The Company is currently developing its first product offering and has no products that have received regulatory approval. To achieve profitable operations, the Company must successfully develop, test, manufacture and market its products. There can be no assurance that any such products can be developed successfully or manufactured at an acceptable cost and with appropriate performance characteristics, or that such products will be successfully marketed. These factors could have a material adverse effect on the Company's future financial results.

Property and equipment

Property and equipment is stated at cost less accumulated depreciation. Depreciation is computed on a straight-line basis over the estimated useful lives of the related assets, generally three years. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is reflected in operations.

Impairment of long-lived assets

In accordance with the provisions of Statement of Financial Accounting Standards Board ("SFAS") No. 144, "Accounting for the Impairment or Disposal of Long-lived Assets," the Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Under SFAS No. 144, an impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. Impairment, if any, is measured as the amount by which the carrying amount of a long-lived asset exceeds its fair value. The Company considers various valuation factors, principally discounted cash flows, to assess the fair values of long-lived assets. As of December 31, 2003, the Company has not incurred such impairment losses.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

Comprehensive income (loss)

Comprehensive income (loss) generally represents all changes in stockholders' deficit except those resulting from investments or contributions by stockholders. The Company's unrealized gain (loss) on available-for-sale marketable securities represents the only component of other comprehensive loss.

Unaudited pro forma stockholders' equity

If the offering contemplated by this prospectus is closed, all of the redeemable convertible preferred stock outstanding will automatically convert into 33,848,484 shares of common stock based on the shares of redeemable convertible preferred stock outstanding at September 30, 2004. Unaudited pro forma stockholders' equity, as adjusted for the assumed conversion of the redeemable convertible preferred stock, is set forth on the balance sheet.

Research and development expenditures

Research and development costs are charged to research and development expense as incurred. Cost accruals for preclinical and clinical studies are based upon estimates of work completed under service agreements, milestones achieved and services performed. The Company's estimates of work completed and associated cost accruals include its assessments of information received from third-party contract research organizations and the overall status of preclinical and clinical trial activities.

Advertising costs

Advertising costs will be expensed as incurred. The Company has not incurred any advertising costs since its inception.

Income taxes

The Company accounts for income taxes under the liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

Segments

The Company operates in one segment, using one measurement of profitability to manage its business. All long-lived assets are maintained in the United States of America.

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THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

Net loss per common share

Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of vested common shares outstanding during the period. Diluted net loss per common share is computed by giving effect to all potential dilutive common shares, including options, common stock subject to repurchase, warrants and redeemable convertible preferred stock. A reconciliation of the numerator and denominator used in the calculation of basic and diluted net loss per common share follows (in thousands):

	Period from October 17, 2001 (date of inception) to December 31, 2001	Years Ended December 31,		Nine Months Ended September 30,	
	2001	2002	2003	2003	2004
				(unaudited)	
Numerator:					
Net loss	\$ (236)	\$(2,458)	\$ (8,303)	\$(6,466)	\$(15,703)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	(40,862)	—	—
Net loss attributable to common stockholders	\$ (236)	\$(2,458)	\$(49,165)	\$(6,466)	\$(15,703)
Denominator:					
Weighted-average number of common shares outstanding	224	286	301	299	3,228
Less: Weighted-average shares subject to repurchase	(41)	(170)	(140)	(141)	(2,255)
Weighted-average number of common shares outstanding used in computing basic and diluted net loss per common share	183	116	161	158	973

The following outstanding options, common stock subject to repurchase, redeemable convertible preferred stock and warrants were excluded from the computation of diluted net loss per common share for the periods presented because including them would have had an antidilutive effect (in thousands):

	December 31,			September 30,	
	2001	2002	2003	2003	2004
				(unaudited)	
Redeemable convertible preferred stock	250	9,000	33,848	9,000	33,848
Options to purchase common stock	—	1,775	2,949	2,939	860
Common stock subject to repurchase	162	157	125	131	3,145
Warrants to purchase redeemable convertible preferred stock	—	—	38	38	38

Stock-based compensation

The Company uses the intrinsic value method of Accounting Principles Board Opinion No. 25 "Accounting for Stock Issued to Employees," ("APB No. 25") in accounting for its employee stock options, and presents disclosure of pro forma information required under SFAS No. 123, "Accounting for Stock-Based Compensation

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THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

(“SFAS No. 123”), as amended by SFAS No. 148, “Accounting for Stock-Based Compensation—Transition and Disclosure—an amendment of FASB Statement No. 123” (“SFAS No. 148”).

If compensation expense had been determined based upon the fair value at the grant date for employee compensation arrangements, consistent with the methodology prescribed under SFAS No. 123, the Company’s pro forma net loss attributable to common stockholders and pro forma net loss per common share attributable to common stockholders under SFAS No. 123 would have been as follows (in thousands, except per share data):

	Period from October 17, 2001 (date of inception) to December 31, 2001	Years Ended December 31,		Nine Months Ended September 30,	
		2002	2003	2003	2004
				(unaudited)	
Net loss attributable to common stockholders, as reported	\$ (236)	\$(2,458)	\$(49,165)	\$(6,466)	\$(15,703)
Add: Employee stock-based compensation included in reported net loss	—	1	810	665	3,422
Deduct: Employee total stock-based compensation determined under fair value method	—	(13)	(815)	(670)	(2,345)
Pro forma net loss attributable to common stockholders	\$ (236)	\$(2,470)	\$(49,170)	\$(6,471)	\$(14,626)
Net loss attributable to common stockholders per common share, basic and diluted:					
As reported	\$ (1.29)	\$(21.19)	\$(305.37)	\$(40.92)	\$ (16.14)
Pro forma	\$ (1.29)	\$(21.29)	\$(305.40)	\$(40.96)	\$ (15.03)

Differences may not be representative of future compensation costs because options vest over several years and additional grants are made each year.

In accordance with the provisions of SFAS No. 123, the fair value of each option is estimated using the minimum value method based on the following assumptions:

	Years Ended December 31,		Nine Months Ended September 30,	
	2002	2003	2003	2004
			(unaudited)	
Weighted average risk-free interest rate	2.98%	1.98%	1.98%	4.27%
Expected life (in years)	4	4	4	4
Dividend yield	—	—	—	—

The grant date weighted average fair value per share of options granted during the years ended December 31, 2002 and 2003 and the nine months ended September 30, 2004 was \$0.03, \$2.11 and \$5.13 (unaudited), respectively. The Company did not grant any options to purchase common stock during the period from October 17, 2001 (date of inception) to December 31, 2001.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

The Company accounts for equity instruments issued to non-employees in accordance with the provisions of SFAS No. 123 and Emerging Issues Task Force (“EITF”) Issue No. 96-18, “Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services” which require that such equity instruments are recorded at their fair value on the measurement date. The measurement of stock-based compensation is subject to periodic adjustment as the underlying equity instruments vest.

Recent accounting pronouncements

In May 2003, the FASB issued SFAS No. 150, “Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity” (“SFAS No. 150”). SFAS No. 150 establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. SFAS No. 150 requires that an issuer classify those financial instruments as liabilities (or assets in some circumstances). Under previous guidance, issuers could account for those financial instruments as equity. SFAS No. 150 is effective for financial instruments entered into or modified after May 31, 2003, and otherwise is effective at the beginning of the first interim period beginning after June 15, 2003. In November 2003, certain elements of SFAS No. 150 were deferred to fiscal periods beginning after December 15, 2004. SFAS No. 150 is to be implemented by reporting the cumulative effect of a change in an accounting principle for financial instruments created before the issuance date of SFAS No. 150 and still existing at the beginning of the interim period of adoption. Restatement is not permitted. The adoption of the effective elements of SFAS No. 150 had no material effect on the Company’s financial position or results of operations. The Company does not expect the adoption of the deferred elements of SFAS No. 150 to have a material effect on its financial position or results of operations.

In December 2003, the FASB issued a revised FASB Interpretation No. 46 (“FIN No. 46R”), “Consolidation of Variable Interest Entities, an interpretation of ARB No. 51.” The FASB published the revision to clarify and amend some of the original provisions of FIN No. 46, which was issued in January 2003, and to exempt certain entities from its requirements. A variable interest entity (“VIE”) refers to an entity subject to consolidation according to the provisions of this Interpretation. FIN No. 46R applies to entities whose equity investment at risk is insufficient to finance that entity’s activities without receiving additional subordinated financial support provided by any parties, including equity holders, or where the equity investors (if any) do not have a controlling financial interest. FIN No. 46R provides that if an entity is the primary beneficiary of a VIE, the assets, liabilities, and results of operations of the VIE should be consolidated in the entity’s financial statements. In addition, FIN No. 46R requires that both the primary beneficiary and all other enterprises with a significant variable interest in a VIE provide additional disclosures. The provisions of FIN No. 46R will be effective in the first quarter of fiscal 2004. The Company does not expect the adoption of FIN No. 46R to have a material effect on its financial position or results of operations.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

NOTE 3—MARKETABLE SECURITIES:

	<u>Cost Basis</u>	<u>Unrealized Gain</u>	<u>Unrealized Loss</u>	<u>Fair Value</u>
As of December 31, 2002 (in thousands):				
Common stock in a public company	\$ 46	\$ —	\$ (1)	\$ 45
As of December 31, 2003 (in thousands):				
Common stock in a public company	\$ 46	\$ 163	\$ —	\$ 209
As of September 30, 2004 (unaudited, in thousands):				
Common stock in a public company	\$ 46	\$ 110	\$ —	\$ 156
Corporate bonds	2,955	—	(3)	2,952
Government securities	5,306	—	(4)	5,302
Commercial paper	4,577	—	(5)	4,572
Total	\$12,884	\$ 110	\$ (12)	\$12,982

NOTE 4—PROPERTY AND EQUIPMENT:

Property and equipment comprise the following (in thousands):

	<u>December 31,</u>	
	<u>2002</u>	<u>2003</u>
Laboratory equipment	\$ 52	\$ 270
Computer equipment	30	30
	82	300
Less: Accumulated depreciation	(11)	(101)
	\$ 71	\$ 199

NOTE 5—ACCRUED LIABILITIES:

Accrued liabilities comprise the following (in thousands):

	<u>December 31,</u>	
	<u>2002</u>	<u>2003</u>
Professional services fees	\$ 50	\$ 125
Payroll and employee related expenses	12	77
Clinical expenses	7	217
Other accrued expenses	34	18
	\$ 103	\$ 437

NOTE 6—NOTES PAYABLE:

On March 27, 2003, the Company entered into a line of credit agreement, as amended, with a financial institution under which the Company can borrow up to \$1,000,000 for working capital requirements and

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equipment purchases through March 31, 2005. Each borrowing under the line of credit accrues interest at the greater of the treasury note rate plus 3.0% or a fixed rate of 5.5% per annum at the date of borrowing and is repayable in 36 monthly installments. As of December 31, 2003, the Company had borrowed \$300,000 under its working capital line of credit and \$210,000 under the equipment line of credit, for borrowings of approximately \$510,000 at an interest rate of 5.5% per annum. Borrowings under the equipment line of credit are collateralized by the related equipment. In connection with the agreement, the Company issued a warrant to purchase 38,000 shares of Series A redeemable convertible preferred stock to the financial institution (see Note 8).

At December 31, 2003, future principal payments under the notes payable are as follows (in thousands):

Year Ending December 31,	
2004	\$ 166
2005	175
2006	67
Total	<u>\$ 408</u>

Under the line of credit agreement, the Company is required to maintain the lower of 85% of its total cash and cash equivalents or \$10,000,000 with the financial institution. At December 31, 2003, the Company was in compliance with this and all other covenants in the agreement.

NOTE 7—COMMITMENTS AND CONTINGENCIES:

On December 18, 2002, the Company entered into a noncancelable facility operating sublease which expires on December 31, 2004. At December 31, 2003, future minimum payments under the lease were \$473,000. In conjunction with the facility lease, the Company issued a standby letter of credit collateralized by a certificate of deposit in lieu of a security deposit for \$85,000. The certificate of deposit is classified as restricted cash (see Note 2).

On August 31, 2004, the Company entered into a noncancelable facility sublease agreement. The lease was effective October 1, 2004 and expires February 2010. The future rental payments required by the Company under all noncancelable operating subleases as of September 30, 2004 are as follows (unaudited, in thousands):

Years Ended December 31,	
Remainder of 2004	\$ 193
2005	384
2006	400
2007	417
2008	518
2009 and thereafter	623
Future minimum rental payments	<u>\$ 2,535</u>

Rent expense for the period from October 17, 2001 (date of inception) to December 31, 2001, for the years ended December 31, 2002 and 2003 and, cumulatively, for the period from October 17, 2001 (date of inception) to December 31, 2003 was \$26,000, \$112,000, \$447,000 and \$585,000, respectively.

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License agreements

In November 2002, the Company entered into an exclusive license agreement with certain individuals for rights to certain patent applications. Under the terms of the agreement, the Company was required to make aggregate upfront payments of approximately \$15,000. Based on the early stage of development and the uncertainty of the feasibility of the licensed technology, the upfront fees were expensed immediately as incurred. The Company is also required to make various milestone payments up to \$700,000 in connection with regulatory filings and approvals and additional royalty payments upon product commercialization. No milestone or royalty payments have been made as of December 31, 2003.

In June 2004, the Company entered into an agreement with Acraf, S.p.a. for rights to use Acraf's regulatory documents and pre-clinical and clinical information pertaining to the active ingredient in TH-070 for the Company's regulatory filings on TH-070-based products and for obtaining marketing authorizations world-wide for such products. In consideration for the licenses under this agreement, the Company paid Acraf a one-time payment of €300,000, or approximately \$374,000, in 2004. The Company is also obligated to pay Acraf milestone payments, with the next such milestone payment due in connection with the marketing approval of the first TH-070-based product in certain specified territories. In addition, there is a sales-based milestone due should sales of a Company product containing TH-070 exceed €50 million in one year. Future aggregate milestone payments under this agreement could total €1.8 million.

In August 2003, the Company entered into an exclusive worldwide license and development agreement with a corporation for certain patent rights and technology. Under the terms of the agreement, the Company made an initial upfront payment of \$100,000 and as of December 31, 2003, the Company has made a milestone payment of \$100,000. In November 2004, the Company made an additional milestone payment of \$1.3 million. Total additional milestone payments in connection with the development of glufosfamide and United States of America and foreign regulatory submissions and approvals could equal \$8.0 million. In addition, based on the attainment of specified sales thresholds the Company could be required to make payments totaling \$17.5 million. The Company will also be required to make royalty payments upon product commercialization. No royalty payments have been made as of December 31, 2003.

In November 2004, the Company entered into a Development Agreement with MediBIC Co. Ltd. Under this agreement, the Company is due to receive an upfront payment of \$4.75 million to support the development of glufosfamide in the Asian countries covered by the agreement and an option payment of \$250,000. The Company will be required to refund these payments and the agreement will terminate if the Company and MediBIC cannot agree to the development plan by March 1, 2005, or a later date agreed by the parties. The Company is responsible for all development activities and MediBIC has no other funding obligations. The Company will also be required to make royalty payments upon product commercialization. The Company may terminate the agreement at any time by making certain payments to MediBIC ranging from \$5.25 to \$15 million, depending on the stage of development. The Chief Operating Officer and a director of Anexus Pharmaceuticals, Inc., a subsidiary of Med-BIC, is the wife of the Company's Chief Executive Officer.

Indemnification

The Company enters into indemnification provisions under its agreements with other companies in the ordinary course of business, including business partners, contractors and parties performing its clinical trials. Pursuant to these arrangements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified parties for losses suffered or incurred by the indemnified party as a result of the Company's activities. The terms of these indemnification agreements are generally perpetual. The maximum potential amount of future payments the Company could be required to make under these agreements is not determinable. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. As a result, the Company believes the estimated fair value of these agreements is minimal. The

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Company maintains commercial general liability insurance and products liability insurance to offset certain of its potential liabilities under these indemnification provisions.

The Company's bylaws provide that it is required to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct of a culpable nature to the fullest extent permissible by applicable law; and to advance their expenses incurred as a result of any proceeding against them as to which they could be indemnified. As of December 31, 2003, the Company did not have directors' and officers' insurance.

NOTE 8—REDEEMABLE CONVERTIBLE PREFERRED STOCK:

Under the Company's Certificate of Incorporation, as amended, the Company is authorized to issue preferred stock in series. The Company's Board of Directors is authorized to determine the rights, preferences and terms of each series.

As of December 31, 2001, the redeemable convertible preferred stock comprises:

	Number of Shares Designated and Authorized	Number of Shares Issued and Outstanding	Carrying Value	Liquidation Value per Share
Series A	9,500,000	250,000	\$ 236,000	\$ 1.00

As of December 31, 2002, the redeemable convertible preferred stock comprises:

	Number of Shares Designated and Authorized	Number of Shares Issued and Outstanding	Carrying Value	Liquidation Value per Share
Series A	9,500,000	9,000,000	\$ 8,977,000	\$ 1.00

As of December 31, 2003 and September 30, 2004 (unaudited), the redeemable convertible preferred stock comprises:

	Number of Shares Designated and Authorized	Number of Shares Issued and Outstanding	Carrying Value	Liquidation Value per Share
Series A	9,038,000	9,000,000	\$ 8,977,000	\$ 1.00
Series B	24,848,484	24,848,484	40,862,000	\$ 1.65
	<u>33,886,484</u>	<u>33,848,484</u>	<u>\$ 49,839,000</u>	

On November 14, 2003, the Company amended its Certificate of Incorporation to increase the total number of authorized shares of redeemable convertible preferred stock to 33,886,484, of which 9,038,000 and 24,848,484 shares have been designated as Series A and B redeemable convertible preferred stock, respectively. As part of the amendment, the Company re-designated 462,000 shares of unissued Series A redeemable convertible preferred stock into authorized Series B redeemable convertible preferred stock.

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As of December 31, 2003, the rights, preferences, privileges and restrictions of Series A and B redeemable convertible preferred stock are:

Dividends

The holders of the Series B redeemable convertible preferred stock are entitled to receive noncumulative annual dividends at the rate of \$0.132 per share when, as and if declared by the Board of Directors. Dividends on Series B redeemable convertible preferred stock shall be payable in preference to and prior to payment of dividends on Series A redeemable convertible preferred stock and common stock. If Series B redeemable convertible preferred stock have been paid in full or declared and set apart, the holders of the Series A redeemable convertible preferred stock are entitled to receive noncumulative annual dividends at the rate of \$0.08 per share when, as and if declared by the Board of Directors. Dividends on Series A redeemable convertible preferred stock shall be payable in preference to and prior to payment of dividends on common stock. In the event that dividends are paid on common stock, dividends shall be paid on redeemable convertible preferred stock in an amount equal per share (on an as-if-converted basis) to the amount paid for each share of common stock. As of September 30, 2004 (unaudited), no dividends had been declared on any class of the Company's capital stock.

Liquidation

A merger, consolidation or sale of all or substantially all of the assets of the Company which will result in the Company's stockholders immediately prior to such transaction holding less than 50% of the voting power of the surviving, continuing or purchasing entity will be deemed to be a liquidation, dissolution or winding up of the Company.

In the event of any liquidation or winding up of the Company, the holders of the Company's Series B redeemable convertible preferred stock are entitled to receive, prior to any distribution of the Company's assets to and in preference to any distribution to holders of Series A redeemable convertible preferred stock and common stock, an amount equal to \$1.65 per share for each outstanding share of Series B redeemable convertible preferred stock, plus any declared but unpaid dividends. If the Company's assets are insufficient to provide for such preferential distributions, the holders of Series B redeemable convertible preferred stock will receive all of the Company's remaining assets on a pro rata basis.

After distributions have been made to the holders of Series B redeemable convertible preferred stock, the holders of the Company's Series A redeemable convertible preferred stock will be entitled to receive, prior to any distribution of the Company's assets to and in preference to any distribution to holders of the common stock, an amount equal to \$1.00 per share for each outstanding share of Series A redeemable convertible preferred stock, plus any declared but unpaid dividends. If the Company's assets are insufficient to provide for such preferential distributions, the holders of Series A redeemable convertible preferred stock will receive all of the Company's remaining assets on a pro rata basis.

Following full payment to the holders of Series A and B redeemable convertible preferred stock, the holders of common stock will be entitled to the remaining assets, if any, on a pro rata basis.

Redemption

The merger or consolidation of the Company into another entity or any transactions in which more than 50% of the voting power of the Company is disposed of or the sale, transfer or disposition of substantially all of the

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property or business of the Company is deemed a liquidation, dissolution, or winding up of the Company. These liquidation characteristics require classification of the redeemable convertible preferred stock outside of the stockholders' deficit section as these factors are outside the control of the Company. The redeemable convertible preferred stock is not redeemable in any other circumstances.

Conversion

Each share of redeemable convertible preferred stock, at the option of the holder, is convertible at any time into the number of fully paid and nonassessable shares of common stock (adjusted to reflect stock dividends, stock splits and recapitalization) that results from dividing the original issue price by the conversion price in effect at the time of the conversion. The original issue price of the Series A and B redeemable convertible preferred stock is \$1.00 and \$1.65 per share, respectively. The initial per share conversion price of the Series A and B redeemable convertible preferred stock is \$1.00 and \$1.65 per share, respectively.

If not previously converted at the option of the holder, the conversion of the convertible preferred stock is automatic and will be converted at the then applicable prices upon the earlier of any of the following events: (i) affirmative election of the holders of at least 75% of the then outstanding shares of the redeemable convertible preferred stock, or (ii) the closing of a firm commitment underwritten public offering based on an effective registration statement under the Securities Act of 1933 for the issuance of common stock. The aggregate proceeds raised from the offering must exceed \$50,000,000 prior to the underwriters' commission and other offering costs, and with a pre-money valuation not less than \$200,000,000.

Voting rights

The holder of each share of the Company's redeemable convertible preferred stock has the right to one vote for each share of common stock into which such redeemable convertible preferred stock could be converted.

As long as at least 6,000,000 shares of Series B redeemable convertible preferred stock remain outstanding, the Company must obtain approval from at least 60% of the then outstanding shares of Series B redeemable convertible preferred stock in order to amend the Certificate of Incorporation or Bylaws as related to Series B redeemable convertible preferred stock, or change or reclassify any shares of redeemable convertible preferred stock that adversely effects the rights, preferences or privileges relating to Series B redeemable convertible preferred stock.

As long as at least 4,000,000 shares of Series A redeemable convertible preferred stock remain outstanding, the Company must obtain approval from a majority of the then outstanding shares of Series A redeemable convertible preferred stock in order to amend the Certificate of Incorporation or Bylaws as related to Series A redeemable convertible preferred stock, or change or reclassify any shares that adversely effects the rights, preferences or privileges relating to Series A redeemable convertible preferred stock.

As long as at least 8,462,121 shares of Series A and Series B redeemable convertible preferred stock remain outstanding, the Company must obtain approval from at least 75% of the then outstanding Series A and Series B redeemable convertible preferred shares in order to change the authorized number of shares of common stock or redeemable convertible preferred stock, take actions that result in certain redemption or repurchase of any shares of common stock, result in a consolidation, merger or asset sale, declare or pay dividends, enter into a consolidation or sale of substantially all of its assets, or issue debt in excess of \$500,000.

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Sale of Series B redeemable convertible preferred securities

In November 2003, the Company sold an aggregate of 24,848,484 shares of Series B redeemable convertible preferred stock for net proceeds of approximately \$40,862,000. The issuance of Series B redeemable convertible preferred stock resulted in a beneficial conversion feature, calculated in accordance with EITF No. 00-27, "Application of Issue No. 98-5, "Accounting for Convertible Securities with Beneficial Conversion Features of Contingently Adjustable Conversion Ratios" to Certain Convertible Instruments" based upon the conversion price of the preferred stock into common, and the fair value of the common stock at the date of issue. Accordingly, the Company has recognized approximately \$40,862,000 as a charge to additional paid-in-capital to account for the deemed dividend on the redeemable convertible preferred stock as of the issuance date in the year ended December 31, 2003. In accordance with the provisions of EITF No. 00-27, the amount of the deemed dividend related to the beneficial conversion feature is limited to the net proceeds received by the Company for the sale of the related securities and was recorded upon issuance of the Series B redeemable convertible preferred stock, as the Series B redeemable convertible preferred stock can be converted to common stock by the holder at any time.

Warrant

In connection with the line of credit agreement in March 2003, the Company issued a warrant to purchase an aggregate of 38,000 shares of Series A redeemable convertible preferred stock at an exercise price of \$1.00 per share. The warrant was fully vested and exercisable upon grant, and will expire in March 2013 or seven years after the closing date of the Company's initial public offering, whichever is later. At the date of issuance, the aggregate fair value of the warrant was deemed to be \$44,000, which was determined using the Black-Scholes valuation model with the following assumptions: term of 10 years, risk free rate of 4.33%, volatility of 70% and a dividend yield of zero. The fair value of the warrant has been reflected as an other asset and is being amortized to interest expense on a straight-line basis over the term of the line of credit.

NOTE 9—STOCKHOLDERS' DEFICIT:

Common stock

Each share of common stock has the right to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when declared by the Board of Directors, subject to the prior rights of holders of all classes of stock outstanding having priority rights as to dividends. No dividends have been declared or paid as of December 31, 2003.

On October 24, 2001, shares of restricted stock were issued to the Company's founder and member of the Board of Directors under a restricted stock purchase agreement. On January 29, 2002, shares of restricted common stock were issued to a member of the Board of Directors under a restricted stock purchase agreement. Generally, the shares vest over a four-year period. The unvested shares of common stock are subject to repurchase by the Company in the event of termination of the employment or consulting relationship. Included in common stock as of December 31, 2002 and 2003 and September 30, 2004 are 157,061, 125,116 and 98,842 (unaudited) shares subject to the Company's right of repurchase, respectively.

2001 Equity Incentive Plan

In December 2001, as amended in November 2003, the Board of Directors authorized the 2001 Stock Plan (the "2001 Plan") under which the Company may issue incentive stock options and nonstatutory stock options.

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As of December 31, 2003, the Company has reserved 7,000,000 shares of common stock for issuance under the 2001 Plan. Options may be granted at an exercise price not less than fair market value for incentive stock options and not less than 85% of fair market value for nonstatutory stock options. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive and nonstatutory stock options may not be less than 110% of fair market value. The options may be exercised, in whole or in part, upon grant and generally vest over a four-year period. The 2001 Plan requires that options be exercised no later than ten years after the date of the grant. Included in common stock at September 30, 2004 are 3,045,717 (unaudited) shares subject to repurchase relating to options exercised prior to vesting.

Activity under the 2001 Plan is set forth below:

	Shares Available for Grant	Outstanding Options		Weighted Average Exercise Price
		Number of Shares	Exercise Price	
Shares reserved at Plan inception	2,000,000	—	\$ —	\$ —
Balances, December 31, 2001	2,000,000	—	—	—
Options granted	(1,778,692)	1,778,692	0.10	0.10
Options exercised	—	(4,000)	0.10	0.10
Balances, December 31, 2002	221,308	1,774,692	0.10	0.10
Additional shares reserved	5,000,000	—	—	—
Options granted	(1,196,577)	1,196,577	0.10–0.16	0.10
Options exercised	—	(12,702)	0.10	0.10
Options canceled	9,170	(9,170)	0.10	0.10
Balances, December 31, 2003	4,033,901	2,949,397	0.10–0.16	0.10
Options granted (unaudited)	(3,233,000)	3,233,000	0.16–0.32	0.20
Options exercised (unaudited)	—	(5,243,845)	0.10–0.32	0.13
Options canceled (unaudited)	78,321	(78,321)	0.10–0.32	0.11
Balances, September 30, 2004 (unaudited)	879,222	860,231	\$ 0.10–0.32	\$ 0.28

The number of options outstanding at September 30, 2004 includes 437,000 (unaudited) unvested options granted and exercised that are not considered to be exercised for accounting purposes in accordance with EITF Issue No. 00-23, “Issues Related to the Accounting for Stock Compensation under APB Opinion No. 25 and FASB Interpretation No. 44.”

The number of options outstanding and vested at December 31, 2002 was 726,671 shares with a weighted- average exercise price of \$0.10 per share.

At December 31, 2003, stock options outstanding and vested by exercise price are as follows:

Options Outstanding and Exercisable			Options Vested	
Exercise Price	Number of Options Outstanding	Weighted Average Remaining Contractual Life (Years)	Number Vested	Weighted Average Exercise Price
\$0.10	2,939,397	9.21	1,518,843	\$ 0.10
\$0.16	10,000	9.92	208	0.16
	2,949,397		1,519,051	\$ 0.10

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At September 30, 2004 (unaudited), stock options outstanding and vested by exercise price are as follows:

Options Outstanding and Exercisable			Options Vested	
Exercise Price	Number of Options Outstanding	Weighted Average Remaining Contractual Life (Years)	Number Vested	Weighted Average Exercise Price
\$0.10	122,855	8.03	231,153	\$ 0.10
\$0.16	44,376	9.44	149,969	0.16
\$0.32	693,000	9.61	18,906	0.32
	<u>860,231</u>		<u>400,028</u>	<u>\$ 0.13</u>

Deferred stock-based compensation

During the years ended December 31, 2002 and 2003 and the nine months ended September 30, 2003 and 2004, the Company issued options to certain employees under the 2001 Plan with exercise prices below the fair market value of the Company's common stock at the date of grant, determined with hindsight. In accordance with the requirements of APB No. 25, the Company has recorded deferred stock-based compensation for the difference between the exercise price of the stock option and the fair market value of the Company's stock at the date of grant. This deferred stock-based compensation is amortized to expense on a straight-line basis over the period during which the Company's right to repurchase the stock lapses or the options vest, generally four years. During the years ended December 31, 2002 and 2003 and the nine months ended September 30, 2003 and 2004, the Company has recorded deferred stock-based compensation related to these options of approximately \$25,000, \$2,332,000, \$2,294,000 (unaudited) and \$11,986,000 (unaudited), net of cancellations, respectively.

During May 2004, the Company granted 637,000 (unaudited) options to employees to purchase shares of common stock at \$0.32 per share. These options contain a call feature that allows the Company to cancel the options by January 31, 2005 if the Company does not complete an initial public offering by December 31, 2004. On December 14, 2004, the Company's Board of Directors eliminated the Company's call feature (unaudited). If the Company elects to exercise this call feature, the outstanding options will be cancelled and any shares purchased pursuant to exercise of the options will be immediately repurchasable by the Company at the original purchase price. The Company has applied the provisions of EITF Issue No. 00-23 and applied variable accounting to these options, resulting in deferred stock-based compensation of \$6,134,000 and stock compensation expense of \$1,505,000 during the nine months ended September 30, 2004 (unaudited). Stock compensation expense has been amortized in accordance with the provisions of FASB Interpretation No. 28, "Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans" for these awards subject to variable accounting. At September 30, 2004, 437,000 (unaudited) of these options had been exercised at \$0.32 per share and were subject to the repurchase feature. The aggregate proceeds of \$140,000 (unaudited) from the exercise of these options is included within liabilities and excluded from earnings per share calculations in accordance with EITF Issue No. 00-23, based upon the Company's right to repurchase the shares at their original exercise price.

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The Company granted stock options to employees with exercise prices below estimated fair market value on the date of grant as follows (unaudited):

Grants Made During Quarter Ended	Number of Options Granted (000's)	Weighted- Average Exercise Price Per Share	Weighted- Average Fair Value Per Share	Weighted- Average Intrinsic Value Per Share
December 31, 2002	166	\$ 0.10	\$ 0.25	\$ 0.15
March 31, 2003	25	0.10	0.82	0.72
June 30, 2003	1,058	0.10	2.20	2.10
September 30, 2003	20	0.10	3.12	3.02
December 31, 2003	10	0.16	3.98	3.82
March 31, 2004	2,309	0.16	4.85	4.69
June 30, 2004	822	0.32	6.55	6.23
September 30, 2004	3	0.32	8.25	7.93

Stock-based compensation expense related to options granted to employees was allocated to research and development and general and administrative as follows (in thousands):

	Years Ended December 31,		Nine Months Ended September 30,	
	2002	2003	2003	2004
Research and development	\$ —	\$ 57	\$ 39	\$ 1,485
General and administrative	1	753	626	1,937
	<u>\$ 1</u>	<u>\$810</u>	<u>\$665</u>	<u>\$ 3,422</u>

Stock-based compensation expense related to stock options granted to non-employees is recognized on a straight-line basis, as the stock options are earned. During the years ended December 31, 2002 and 2003 and the nine months ended September 30, 2004 (unaudited), the Company issued options to non-employees. The options generally vest ratably over three or four years. The values attributable to these options are amortized over the service period and the unvested portion of these options were remeasured at each vesting date. The Company believes that the fair value of the stock options is more reliably measurable than the fair value of the services received. The fair value of the stock options granted were revalued at each reporting date using the Black-Scholes option pricing model as prescribed by SFAS No. 123 using the following assumptions:

	Years Ended December 31,		Nine Months Ended September 30,	
	2002	2003	2003	2004
Risk-free interest rate	4.76%	4.26%	4.26%	4.50%
Expected life (in years)	10	10	10	10
Dividend yield	—	—	—	—
Expected volatility	70%	70%	70%	70%

The stock-based compensation expense will fluctuate as the deemed fair market value of the common stock fluctuates. In connection with the grant of stock options to non-employees, the Company recorded stock-based compensation of approximately \$21,000, \$256,000, \$192,000 (unaudited) and \$396,000 (unaudited) for the years

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ended December 31, 2002 and 2003 and the nine months ended September 30, 2003 and 2004, respectively. The Company did not grant any options to purchase common stock during the period from October 17, 2001 (date of inception) to December 31, 2001. Stock-based compensation expenses related to options granted to non-employees were entirely expensed to research and development.

NOTE 10—INCOME TAXES:

The tax effects of temporary differences that give rise to significant components of the net deferred tax asset are as follows (in thousands):

	December 31,	
	2002	2003
Capitalized start-up costs	\$ 126	\$ 605
Net operating loss carryforwards	947	3,407
Research and development credits	88	385
Other	4	49
Total deferred tax assets	1,165	4,446
Less: Valuation allowance	(1,165)	(4,446)
	\$ —	\$ —

At December 31, 2003, the Company had federal and state net operating loss carryforwards of approximately \$8,592,000 and \$8,328,000 available to offset future regular taxable income. The Company's federal and state net operating loss carryforwards will begin to expire in various amounts in 2021 and 2011, respectively, if not used before such time to offset future taxable income or tax liabilities. For federal and state income tax purposes, a portion of the Company's net operating loss carryforward is subject to certain limitations on annual utilization in case of changes in ownership, as defined by federal and state tax laws.

At December 31, 2003, the Company has research credit carryforwards of approximately \$227,000 and \$239,000 for federal and state income tax purposes, respectively. If not utilized, the federal carryforwards will expire in various amounts beginning in 2011. The California credit can be carried forward indefinitely.

The Company has established a valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets. Management evaluates on a periodic basis the recoverability of deferred tax assets. At such time as it is determined that it is more likely than not that deferred tax assets are realizable, the valuation allowance will be reduced.

NOTE 11—EMPLOYEE BENEFIT PLAN:

In November 2002, the Company implemented a 401(k) Plan to provide a retirement savings program for the employees of the Company. The 401(k) Plan is maintained for the exclusive purpose of benefiting the 401(k) Plan participants. The 401(k) Plan is intended to operate in accordance with all applicable state and federal laws and regulations and, to the extent applicable, the provisions of Department of Labor regulations issued pursuant to ERISA Section 404(c). As of December 31, 2003, the Company did not make any contributions to the 401(k) Plan.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

NOTE 12—SUBSEQUENT EVENTS:

Initial Public Offering

On April 7, 2004, the Board of Directors authorized management of the Company to file a registration statement with the Securities and Exchange Commission permitting the Company to sell shares of its common stock to the public. If the initial public offering is closed under the terms presently anticipated, all of the redeemable convertible preferred stock outstanding will automatically convert into shares of common stock.

2004 Equity Incentive Plan

On April 7, 2004, the Board of Directors adopted the 2004 Equity Incentive Plan (the “2004 Plan”), subject to stockholder approval. The 2004 Plan will become effective upon the completion of the Company’s initial public offering and provides for the granting of incentive stock options, nonstatutory stock options, stock appreciation rights, stock awards and cash awards to employees and consultants.

A total of 4,000,000 shares of common stock have been authorized for issuance pursuant to the 2004 Plan, plus any shares which have been reserved but not issued under the 2001 Plan or issued and forfeited after the date of the initial public offering, plus any shares repurchased at or below the original purchase price and any options which expire or become unexercisable after the initial public offering, thereafter plus all shares of common stock restored by the Board of Directors pursuant to the provision of the 2004 Plan that permits options to be settled on a net appreciation basis. The Company will not grant any options under the 2001 Plan after the effectiveness of the 2004 Plan. On January 1, 2005, and annually thereafter, the authorized shares will automatically be increased by a number of shares equal to the lesser of:

- 5% of the number of the Company’s shares issued and outstanding prior to the preceding December 31;
- 2,000,000 shares;
- an amount determined by the Board of Directors.

2004 Employee Stock Purchase Plan

On April 7, 2004, the Board of Directors adopted the 2004 Employee Stock Purchase Plan (the “Purchase Plan”), subject to stockholder approval. The Purchase Plan contains consecutive, overlapping 24 month offering periods. Each offering period includes four six-month purchase periods. The price of the common stock purchased will be the lower of 85% of the fair market value of the common stock at the beginning of an offering period or at the end of the purchase period. The initial offering period will commence on the effective date of the Company’s initial public offering.

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
NOTES TO FINANCIAL STATEMENTS
(Continued)

NOTE 13—PRO FORMA COMMON SHARES OUTSTANDING AND PRO FORMA NET LOSS PER SHARE (UNAUDITED):

Pro forma basic and diluted net loss per common share have been computed to give effect to redeemable convertible preferred stock that will convert to common stock upon the closing of the Company's initial public offering (using the as-converted method) for the year ended December 31, 2003 and the nine months ended September 30, 2004 as if the closing occurred at the beginning of fiscal 2003. A reconciliation of the numerator and denominator used in the calculation of pro forma net loss per common share follows (in thousands, except per share data):

	Year Ended December 31, 2003	Nine Months Ended September 30, 2004
	(unaudited)	
Numerator:		
Net loss	\$ (8,303)	\$ (15,703)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	(40,862)	—
Net loss attributable to common stockholders	\$ (49,165)	\$ (15,703)
Denominator:		
Weighted-average number of shares outstanding used in computing basic and diluted net loss per common share	161	973
Adjustment to reflect the effect of the assumed conversion of the weighted-average number of preferred stock from the date of issuance, basic and diluted	11,995	33,848
Weighted-average number of shares used in computing basic and diluted pro forma net loss per common share	12,156	34,821
Pro forma net loss per common share		
Basic and diluted	\$ (4.04)	\$ (0.45)



Shares

Common Stock

PROSPECTUS

, 2005

Banc of America Securities LLC

CIBC World Markets

Lazard

William Blair & Company

Through and including _____, 2004 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, 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.

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Part II
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 13. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

Our estimated expenses (other than underwriting discounts) payable in connection with the sale of the common stock offered hereby are as follows:

SEC registration fee	\$ 10,927.88
NASD filing fee	9,120.00
NASDAQ National Market listing fee	100,000.00
Printing and engraving expenses	200,000.00
Legal fees and expenses	850,000.00
Accounting fees and expenses	600,000.00
Blue Sky qualification fees and expenses	5,000.00
Transfer agent and registrar fees and expenses	10,000.00
Miscellaneous fees and expenses	99,952.12
	<hr/>
Total	\$ 1,885,000.00

* 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 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 a 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 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 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 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 certificate of incorporation provides for the indemnification of directors and officers to the fullest extent permissible under Delaware law.

The Underwriting Agreement provides that the underwriters are obligated, under certain circumstances, to indemnify directors, officers and controlling persons of the registrant against certain liabilities, including liabilities under the Securities Act of 1933, as amended. Reference is made to the form of Underwriting Agreement filed as Exhibit 1.1 hereto.

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ITEM 15. RECENT SALES OF UNREGISTERED SECURITIES

Set forth below in chronological order is information regarding the number of shares of capital stock, options and warrants issued by us since our inception on October 17, 2001. Also included is the consideration if any received by us for the securities.

There was no public offering in any such transaction and we believe that each transaction was exempt from the registration requirements of the Securities Act of 1933 by reason of Regulation D and Section 4(2) of the 1933 Act, based on the private nature of the transactions and the financial sophistication of the purchasers, all of whom had access to complete information concerning us and acquired the securities for investment and not with a view to the distribution thereof. In addition, we believe that the transactions described below with respect to the issuance of option grants to our employees and exercise of such options were exempt from registration requirements of the 1933 Act by reason of Rule 701 promulgated thereunder.

1. In October 2001, we sold 250,000 shares of common stock to George F. Tidmarsh, M.D., Ph.D., at \$0.01 per share, for an aggregate purchase price of \$2,500.00.
2. In January 2002, we sold 37,500 shares of common stock to a former director at \$0.10 per share, for an aggregate purchase price of \$3,750.00.
3. Between October 2001 and August 2002, we issued 9,000,000 shares of our Series A preferred stock to investors for an aggregate cash consideration of \$9,000,000.
4. In March 2003, in connection with a loan and security agreement, we issued to Silicon Valley Bank a warrant to purchase 38,000 shares of our Series A convertible preferred stock with an exercise price of \$1.00 per share. The warrant expires on the later of March 27, 2013 or seven years after the effective date of this registration statement.
5. In November 2003, we issued 24,848,484 shares of our Series B preferred stock to investors for an aggregate cash consideration of approximately \$41,000,000.
6. As of September 30, 2004, we had granted and issued options to purchase 6,208,269 shares of our common stock with a weighted average price of \$0.24 per share to a number of our employees, directors and consultants pursuant to our 2001 Equity Incentive Plan. As of September 30, 2004, 5,697,547 shares of common stock were issued upon exercise of certain of these options, of which 437,000 shares were subject to a call feature as of September 30, 2004, which call feature has since been cancelled.

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ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

EXHIBIT NUMBER	DESCRIPTION
1.1*	Form of Underwriting Agreement
3.1**	Amended and Restated Certificate of Incorporation of the Registrant
3.2**	Form of Amended and Restated Certificate of Incorporation of the Registrant to be effective upon closing of the offering
3.3**	Bylaws of the Registrant
3.4**	Form of Amended and Restated Bylaws of the Registration to be effective upon closing of the offering
4.1*	Specimen Certificate evidencing shares of common stock
4.2**	Warrant to purchase stock, issued to Silicon Valley Bank on March 27, 2003
4.3**	Amended and Restated Investor Rights Agreement dated as of November 17, 2003 among the Registrant and the parties listed therein
5.1**	Form of Opinion of Heller Ehrman White & McAuliffe LLP
10.1**	2001 Equity Incentive Plan
10.2**	2004 Equity Incentive Plan
10.3*	2004 Employee Stock Purchase Plan
10.4**	Sub-Lease Agreement by and between Thervance, Inc., a Delaware corporation, and the Registrant dated as of December 5, 2002
10.5**	Amended and Restated Lease Agreement by and between HMS Gateway Office L.P., a Delaware limited partnership, and Advanced Medicine, Inc., a Delaware corporation, dated January 1, 2001
10.6†**	Agreement between the Registrant, Baxter International Inc., a Delaware corporation, and Baxter Oncology GmbH, a German corporation, dated as of August 5, 2003
10.7†**	Exclusive License Agreement by and between the Registrant, Dr. Theodore Lampidis and Dr. Waldemar Priebe, dated as of November 11, 2002
10.8**	Loan and Security Agreement by and between the Registrant and Silicon Valley Bank, dated March 27, 2003
10.9**	Form of Indemnification Agreement by and between the Registrant and its officers and directors
10.10†**	Agreement by and between the Registrant and Aziende Chimiche Riunite Angelini Francesco - Acraf S.p.a. dated as of June 24, 2004
10.11**	Sublease by and between the Registrant and ArQule, Inc. dated as of August 31, 2004
10.12**	Offer Letter by and between the Registrant and William A. Halter dated as of September 3, 2004
10.13**	Offer Letter by and between the Registrant and George G.C. Parker dated as of September 3, 2004
10.14†**	Development Agreement by and between the Registrant and MediBIC Co. Ltd., dated as of November 30, 2004
10.15	Form of Change of Control Severance Agreement by and between the Registrant and each of Harold E. Selick, Janet I. Swearson and Mark G. Matteucci
10.16	Change of Control Severance Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004

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EXHIBIT NUMBER	DESCRIPTION
10.17	Stock Vesting Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
23.2**	Consent of Heller Ehrman White & McAuliffe LLP (included in Exhibit 5.1)
24.1**	Powers of Attorney

* To be filed by amendment

** Previously filed.

† Confidential treatment request as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

ITEM 17. UNDERTAKINGS

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.

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 in 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 of 1933 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 Securities Act of 1933 and will be governed by the final adjudication of such issue.

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 a registration statement in reliance upon Rule 430A and contained in the 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 offerings 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 of 1933, as amended, Threshold Pharmaceuticals, Inc., has duly caused this Amendment No. 4 to Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 28th day of December, 2004.

THRESHOLD PHARMACEUTICALS, INC.

By: /s/ HAROLD E. SELICK
Harold E. Selick
Chief Executive Officer

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POWER OF ATTORNEY

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ HAROLD E. SELICK</u>		December 28, 2004
Harold E. Selick	Director and Chief Executive Officer (principal executive officer)	
<u>*</u>	Chief Financial Officer (principal financial and accounting officer)	December 28, 2004
<u>Janet I. Swearson</u>		
*	Founder, Director and President	December 28, 2004
<u>George F. Tidmarsh</u>		
*	Director	December 28, 2004
<u>Michael F. Powell</u>		
*	Director	December 28, 2004
<u>Ralph E. Christoffersen</u>		
*	Director	December 28, 2004
<u>Patrick G. Enright</u>		
*	Director	December 28, 2004
<u>Wilfred E. Jaeger</u>		
*	Director	December 28, 2004
<u>William A. Halter†</u>		
*	Director	December 28, 2004
<u>George G. C. Parker†</u>		
<u>*/s/ HAROLD E. SELICK</u>		
Attorney in fact		

EXHIBIT INDEX

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* To be filed by amendment

** Previously filed.

† Confidential treatment request as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

THRESHOLD PHARMACEUTICALS, INC.
CHANGE OF CONTROL SEVERANCE AGREEMENT

The Change of Control Severance Agreement (the "Agreement") is made and entered into effective as of _____ (the "Effective Date"), by and between _____ (the "Employee") and Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Company"). Certain capitalized terms used in this Agreement are defined in Section 1 below.

RECITALS

A. It is expected that the Company from time to time will consider the possibility of a Change of Control. The Board of Directors of the Company (the "Board") recognizes that such consideration can be a distraction to the Employee and can cause the Employee to consider alternative employment opportunities.

B. The Board believes that it is in the best interests of the Company and its stockholders to provide the Employee with an incentive to continue Employee's employment and to maximize the value of the Company upon a Change of Control for the benefit of its stockholders.

C. In order to provide the Employee with enhanced financial security and sufficient encouragement to remain with the Company notwithstanding the possibility of a Change of Control, the Board believes that it is imperative to provide the Employee with certain severance benefits upon the Employee's termination of employment following a Change of Control.

AGREEMENT

In consideration of the mutual covenants herein contained and the continued employment of Employee by the Company, the parties agree as follows:

1. Definition of Terms. The following terms referred to in this Agreement shall have the following meanings:

(a) Cause. "Cause" shall mean (i) Employee's gross negligence or willful failure substantially to perform his or her duties and responsibilities to the Company or deliberate violation of a Company policy; (ii) Employee's commission of any act of fraud, embezzlement, dishonesty or any other willful misconduct that has caused or is reasonably expected to result in material injury to the Company; (iii) unauthorized use or disclosure by Employee of any proprietary information or trade secrets of the Company or any other party to whom the Employee owes an obligation of nondisclosure as a result of his or her relationship with the Company; or (iv) Employee's willful breach of any of his or her obligations under any written agreement or covenant with the Company. The determination as to whether a Employee is being terminated for Cause shall be made in good faith by the Company and shall be final and binding on the Employee.

(b) Change of Control. “Change of Control” shall mean the occurrence of any of the following events:

(i) the approval by stockholders of the Company of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) more than fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity outstanding immediately after such merger or consolidation;

(ii) the approval by the stockholders of the Company of a plan of complete liquidation of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company’s assets; or

(iii) any “person” (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becoming the “beneficial owner” (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of the Company representing 50% or more of the total voting power represented by the Company’s then outstanding voting securities.

(c) Involuntary Termination. “Involuntary Termination” shall mean (i) without the Employee’s express written consent, a significant reduction of the Employee’s duties, position or responsibilities relative to the Employee’s duties, position or responsibilities in effect immediately prior to such reduction, or the removal of the Employee from such position, duties and responsibilities, unless the Employee is provided with comparable or greater duties, position and responsibilities; (ii) without the Employee’s express written consent, a substantial reduction, without good business reasons, of the facilities and perquisites (including office space and location) available to the Employee immediately prior to such reduction; (iii) without the Employee’s express written consent, a reduction by the Company of the Employee’s base salary as in effect immediately prior to such reduction; (iv) without the Employee’s express written consent, a material reduction by the Company in the kind or level of employee benefits to which the Employee is entitled immediately prior to such reduction, with the result that the Employee’s overall benefits package is significantly reduced; (v) without the Employee’s express written consent, the imposition of a requirement for the relocation of the Employee to a facility or a location more than fifty (50) miles from the Employee’s current work location; (vi) any purported termination of the Employee’s employment by the Company which is not effected for Cause or for which the grounds relied upon are not valid; or (vii) the failure of the Company to obtain the assumption of this Agreement by any successors contemplated in Section 6 below.

(d) Termination Date. “Termination Date” shall mean the effective date of any notice of termination delivered by one party to the other hereunder.

2. Term of Agreement. Other than Section 4(b) of this Agreement which shall survive indefinitely until all obligations under such Section have been satisfied, this Agreement shall terminate upon the earlier of (i) two (2) years after a Change of Control, or (ii) the date that all obligations of the parties hereto under this Agreement have been satisfied.

3. At-Will Employment. The Company and the Employee acknowledge that the Employee’s employment is and shall continue to be at-will, as defined under applicable law. If

the Employee's employment terminates for any reason, the Employee shall not be entitled to any payments, benefits, damages, awards or compensation other than as provided by this Agreement, or as may otherwise be established under the Company's then existing employee benefit plans or policies at the time of termination.

4. Severance Benefits

(a) Termination Following a Change of Control. If the Employee's employment with the Company terminates as a result of an Involuntary Termination at any time within eighteen (18) months after a Change of Control, and the Employee signs the release of claims pursuant to Section 7 hereto, Employee shall be entitled to the following severance benefits:

(1) Twelve months of Employee's base salary and any applicable allowances as in effect as of the date of the termination or, if greater, as in effect in the year in which the Change of Control occurs, less applicable withholding, payable in a lump sum within thirty (30) days of the Involuntary Termination;

(2) all stock options granted by the Company to the Employee prior to the Change of Control shall accelerate and become vested under the applicable option agreements to the extent such stock options are outstanding and unexercisable at the time of such termination and all stock subject to a right of repurchase by the Company (or its successor) that was purchased prior to the Change of Control shall have such right of repurchase lapse;

(3) the Employee shall be permitted to exercise all vested (including shares that vest as a result of this Agreement) stock options granted by the Company to the Employee prior to the Change of Control for a period of two (2) years following the Termination Date; and

(4) the same level of Company-paid health (i.e., medical, vision and dental) coverage and benefits for such coverage as in effect for the Employee (and any eligible dependents) on the day immediately preceding the Employee's Termination Date; provided, however, that (i) the Employee constitutes a qualified beneficiary, as defined in Section 4980B(g)(1) of the Internal Revenue Code of 1986, as amended; and (ii) Employee elects continuation coverage pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), within the time period prescribed pursuant to COBRA. The Company shall continue to provide Employee with such Company-paid coverage until the earlier of (i) the date Employee (and his/her eligible dependents) is no longer eligible to receive continuation coverage pursuant to COBRA, or (ii) twelve (12) months from the Termination Date.

(b) Termination Apart from a Change of Control. If (but without duplication with the provisions set forth above in subsection 4(a)(1)) the Employee's employment with the Company terminates as a result of an Involuntary Termination, the Employee shall be entitled to severance benefits in the form of twelve (12) months of Employee's base salary as in effect as of the date of termination, less applicable withholding, payable in a lump sum within thirty (30) days of the Involuntary Termination.

(c) Accrued Wages and Vacation Expenses. Without regard to the reason for, or the timing of, Employee's termination of employment: (i) the Company shall pay the Employee any unpaid base salary due for periods prior to the Termination Date; (ii) the Company shall pay the Employee all of the Employee's accrued and unused vacation through the Termination Date; and (iii) following submission of proper expense reports by the Employee, the Company shall reimburse the Employee for all expenses reasonably and necessarily incurred by the Employee in connection with the business of the Company prior to the Termination Date. These payments shall be made promptly upon termination and within the period of time mandated by law.

5. Limitation on Payments. In the event that the severance and other benefits provided for in this Agreement or otherwise payable to the Employee (i) constitute "parachute payments" within the meaning of Section 280G of the Code, and (ii) would be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then Employee's benefits under this Agreement shall be either

(a) delivered in full, or

(b) delivered as to such lesser extent which would result in no portion of such benefits being subject to the Excise Tax,

whichever of the foregoing amounts, taking into account the applicable federal, state and local income taxes and the Excise Tax, results in the receipt by Employee on an after-tax basis, of the greatest amount of benefits, notwithstanding that all or some portion of such benefits may be taxable under Section 4999 of the Code.

Unless the Company and the Employee otherwise agree in writing, any determination required under this Section shall be made in writing by the Company's independent public accountants (the "Accountants"), whose determination shall be conclusive and binding upon the Employee and the Company for all purposes. For purposes of making the calculations required by this Section, the Accountants may make reasonable assumptions and approximations concerning applicable taxes and may rely on reasonable, good faith interpretations concerning the application of Section 280G and 4999 of the Code. The Company and the Employee shall furnish to the Accountants such information and documents as the Accountants may reasonably request in order to make a determination under this Section. The Company shall bear all costs the Accountants may reasonably incur in connection with any calculations contemplated by this Section.

6. Successors.

(a) Company's Successors. Any successor to the Company (whether direct or indirect and whether by purchase, lease, merger, consolidation, liquidation or otherwise) to all or substantially all of the Company's business and/or assets shall assume the Company's obligations under this Agreement and agree expressly to perform the Company's obligations under this Agreement in the same manner and to the same extent as the Company would be required to perform such obligations in the absence of a succession. For all purposes under this Agreement, the term "Company" shall include any successor to the Company's business and/or assets which executes and delivers the assumption agreement described in this subsection (a) or which becomes bound by the terms of this Agreement by operation of law.

(b) Employee's Successors. Without the written consent of the Company, Employee shall not assign or transfer this Agreement or any right or obligation under this Agreement to any other person or entity. Notwithstanding the foregoing, the terms of this Agreement and all rights of Employee hereunder shall inure to the benefit of, and be enforceable by, Employee's personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees.

7. Execution of Release Agreement upon Termination. As a condition of entering into this Agreement and receiving the benefits under Section 4, the Employee agrees to execute and not revoke a general release of claims upon the termination of employment with the Company.

8. Notices.

(a) General. Notices and all other communications contemplated by this Agreement shall be in writing and shall be deemed to have been duly given when personally delivered or when mailed by U.S. registered or certified mail, return receipt requested and postage prepaid. In the case of the Employee, mailed notices shall be addressed to Employee at the home address which Employee most recently communicated to the Company in writing. In the case of the Company, mailed notices shall be addressed to its corporate headquarters, and all notices shall be directed to the attention of its Chief Executive Officer.

(b) Notice of Termination. Any termination by the Company for Cause or by the Employee as a result of a voluntary resignation shall be communicated by a notice of termination to the other party hereto given in accordance with this Section. Such notice shall indicate the specific termination provision in this Agreement relied upon, shall set forth in reasonable detail the facts and circumstances claimed to provide a basis for termination under the provision so indicated, and shall specify the Termination Date (which shall be not more than 30 days after the giving of such notice). The failure by the Employee to provide the notice or to include in the notice any fact or circumstance which contributes to a showing of Involuntary Termination shall not waive any right of the Employee hereunder or preclude the Employee from asserting such fact or circumstance in enforcing his rights hereunder.

9. Arbitration.

(a) Any dispute or controversy arising out of, relating to, or in connection with this Agreement, or the interpretation, validity, construction, performance, breach, or termination thereof, shall be settled by binding arbitration to be held in Santa Clara, California, in accordance with the National Rules for the Resolution of Employment Disputes then in effect of the American Arbitration Association (the "Rules"). The arbitrator may grant injunctions or other relief in such dispute or controversy. The decision of the arbitrator shall be final, conclusive and binding on the parties to the arbitration. Judgment may be entered on the arbitrator's decision in any court having jurisdiction. The arbitrator may require one party to pay the costs and attorney fees of the prevailing party.

(b) The arbitrator(s) shall apply California law to the merits of any dispute or claim, without reference to conflicts of law rules. The arbitration proceedings shall be governed by federal arbitration law and by the Rules, without reference to state arbitration law. Employee hereby consents to the personal jurisdiction of the state and federal courts located in California for any action or proceeding arising from or relating to this Agreement or relating to any arbitration in which the parties are participants.

(c) Employee understands that nothing in this Section modifies Employee's at-will employment status. Either Employee or the Company can terminate the employment relationship at any time, with or without Cause.

(d) EMPLOYEE HAS READ AND UNDERSTANDS THIS SECTION, WHICH DISCUSSES ARBITRATION. EMPLOYEE UNDERSTANDS THAT SUBMITTING ANY CLAIMS ARISING OUT OF, RELATING TO, OR IN CONNECTION WITH THIS AGREEMENT, OR THE INTERPRETATION, VALIDITY, CONSTRUCTION, PERFORMANCE, BREACH OR TERMINATION THEREOF TO BINDING ARBITRATION, CONSTITUTES A WAIVER OF EMPLOYEE'S RIGHT TO A JURY TRIAL AND RELATES TO THE RESOLUTION OF ALL DISPUTES RELATING TO ALL ASPECTS OF THE EMPLOYER/EMPLOYEE RELATIONSHIP, INCLUDING BUT NOT LIMITED TO, THE FOLLOWING CLAIMS:

(i) ANY AND ALL CLAIMS FOR WRONGFUL DISCHARGE OF EMPLOYMENT; BREACH OF CONTRACT, BOTH EXPRESS AND IMPLIED; BREACH OF THE COVENANT OF GOOD FAITH AND FAIR DEALING, BOTH EXPRESS AND IMPLIED; NEGLIGENT OR INTENTIONAL INFLICTION OF EMOTIONAL DISTRESS; NEGLIGENT OR INTENTIONAL MISREPRESENTATION; NEGLIGENT OR INTENTIONAL INTERFERENCE WITH CONTRACT OR PROSPECTIVE ECONOMIC ADVANTAGE; AND DEFAMATION.

(ii) ANY AND ALL CLAIMS FOR VIOLATION OF ANY FEDERAL STATE OR MUNICIPAL STATUTE, INCLUDING, BUT NOT LIMITED TO, TITLE VII OF THE CIVIL RIGHTS ACT OF 1964, THE CIVIL RIGHTS ACT OF 1991, 1 AGE DISCRIMINATION IN EMPLOYMENT ACT OF 1967, THE AMERICANS WITH DISABILITIES ACT OF 1990, THE FAIR LABOR STANDARDS ACT, THE CALIFORNIA FAIR EMPLOYMENT AND HOUSING ACT, AND LABOR CODE SECTION 20 1, *et seq*;

(iii) ANY AND ALL CLAIMS ARISING OUT OF ANY OTHER LAWS AND REGULATIONS RELATING TO EMPLOYMENT OR EMPLOYMENT DISCRIMINATION.

10. Miscellaneous Provisions.

(a) Effect of Statutory Benefits. To the extent that any severance benefits are required to be paid to the Employee upon termination of employment with the Company as a result of any requirement of law or any governmental entity in any applicable jurisdiction, the aggregate amount of severance benefits payable pursuant to Section 4 hereof shall be reduced by such amount.

(b) No Duty to Mitigate. The Employee shall not be required to mitigate the amount of any payment contemplated by this Agreement, nor shall any such payment be reduced by any earnings that the Employee may receive from any other source.

(c) Waiver. No provision of this Agreement may be modified, waived or discharged unless the modification, waiver or discharge is agreed to in writing and signed by the Employee and by an authorized officer of the Company (other than the Employee). No waiver by either party of any breach of, or of compliance with, any condition or provision of this Agreement by the other party shall be considered a waiver of any other condition or provision or of the same condition or provision at another time.

(d) Integration. This Agreement and any outstanding stock option agreements and any restricted stock purchase agreements referenced herein represent the entire agreement and understanding between the parties as to the subject matter herein and supersede all prior or contemporaneous agreements, whether written or oral, with respect to this Agreement and any stock option agreement or any restricted stock purchase agreement, provided, that, for clarification purposes, this agreement shall not affect any agreements between the Company and Employee regarding intellectual property matters or confidential information of the Company.

(e) Choice of Law. The validity, interpretation, construction and performance of this Agreement shall be governed by the internal substantive laws, but not the conflicts of law rules, of the State of California.

(f) Severability. The invalidity or unenforceability of any provision or provisions of this Agreement shall not affect the validity or enforceability of any other provision hereof, which shall remain in full force and effect.

(g) Employment Taxes. All payments made pursuant to this Agreement shall be subject to withholding of applicable income and employment taxes.

(h) Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together will constitute one and the same instrument.

IN WITNESS WHEREOF, each of the parties has executed this Agreement, in the case of the Company by its duly authorized officer, as of the day and year first above written.

COMPANY:

Threshold Pharmaceuticals, Inc..

By: _____

Title: _____

EMPLOYEE:

Signature

Printed Name

THRESHOLD PHARMACEUTICALS, INC.
CHANGE OF CONTROL SEVERANCE AGREEMENT

The Change of Control Severance Agreement (the "Agreement") is made and entered into effective as of December 23, 2004 (the "Effective Date"), by and between George Tidmarsh (the "Employee") and Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Company"). Certain capitalized terms used in this Agreement are defined in Section 1 below.

RECITALS

A. It is expected that the Company from time to time will consider the possibility of a Change of Control. The Board of Directors of the Company (the "Board") recognizes that such consideration can be a distraction to the Employee and can cause the Employee to consider alternative employment opportunities.

B. The Board believes that it is in the best interests of the Company and its stockholders to provide the Employee with an incentive to continue Employee's employment or participation as an advisor to the Company and to maximize the value of the Company upon a Change of Control for the benefit of its stockholders.

C. In order to provide the Employee with enhanced financial security and sufficient encouragement to remain with the Company notwithstanding the possibility of a Change of Control, the Board believes that it is imperative to provide the Employee with certain severance benefits upon the Employee's termination of employment following a Change of Control.

AGREEMENT

In consideration of the mutual covenants herein contained and the continued employment of Employee by the Company, the parties agree as follows:

1. Definition of Terms. The following terms referred to in this Agreement shall have the following meanings:

(a) Cause. "Cause" shall mean (i) Employee's gross negligence or willful failure substantially to perform his or her duties and responsibilities to the Company or deliberate violation of a Company policy; (ii) Employee's commission of any act of fraud, embezzlement, dishonesty or any other willful misconduct that has caused or is reasonably expected to result in material injury to the Company; (iii) unauthorized use or disclosure by Employee of any proprietary information or trade secrets of the Company or any other party to whom the Employee owes an obligation of nondisclosure as a result of his or her relationship with the Company; or (iv) Employee's willful breach of any of his or her obligations under any written agreement or covenant with the Company. The determination as to whether an Employee is being terminated for Cause shall be made in good faith by the Company and shall be final and binding on the Employee.

(b) Change of Control. "Change of Control" shall mean the occurrence of any of the following events:

(i) the approval by stockholders of the Company of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) more than fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity outstanding immediately after such merger or consolidation;

(ii) the approval by the stockholders of the Company of a plan of complete liquidation of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company's assets; or

(iii) any "person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becoming the "beneficial owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of the Company representing 50% or more of the total voting power represented by the Company's then outstanding voting securities.

(c) Involuntary Termination. "Involuntary Termination" shall mean (i) without the Employee's express written consent, a reduction by the Company of the Employee's base salary as in effect immediately prior to such reduction; (ii) without the Employee's express written consent, a material reduction by the Company in the kind or level of employee benefits to which the Employee is entitled immediately prior to such reduction, with the result that the Employee's overall benefits package is significantly reduced; (iii) without the Employee's express written consent, the imposition of a requirement for the relocation of the Employee to a facility or a location more than fifty (50) miles from the Employee's current work location; (iv) any purported termination of the Employee's employment by the Company which is not effected for Cause or for which the grounds relied upon are not valid; or (v) the failure of the Company to obtain the assumption of this Agreement by any successors contemplated in Section 6 below.

(d) Termination Date. "Termination Date" shall mean the effective date of any notice of termination delivered by one party to the other hereunder.

2. Term of Agreement. Other than Section 4(b) of this Agreement which shall survive indefinitely until all obligations under such Section have been satisfied, this Agreement shall terminate upon the earlier of (i) two (2) years after a Change of Control, or (ii) the date that all obligations of the parties hereto under this Agreement have been satisfied.

3. At-Will Employment. The Company and the Employee acknowledge that the Employee's employment is and shall continue to be at-will, as defined under applicable law. If the Employee's employment terminates for any reason, the Employee shall not be entitled to any payments, benefits, damages, awards or compensation other than as provided by this Agreement, or as may otherwise be established under the Company's then existing employee benefit plans or policies at the time of termination.

4. Severance Benefits.

(a) Termination of Employment Following a Change of Control. If the Employee is an Employee of the Company at the time of a Change of Control and the Employee's employment with the Company terminates as a result of an Involuntary Termination at any time within eighteen (18) months after a Change of Control and the Employee signs the release of claims pursuant to Section 7 hereto, Employee shall be entitled to the following severance benefits:

(1) Twelve months of Employee's base salary and any applicable allowances as in effect as of the date of the termination or, if greater, as in effect in the year in which the Change of Control occurs, less applicable withholding, payable in a lump sum within thirty (30) days of the Involuntary Termination;

(2) all stock options granted by the Company to the Employee prior to the Change of Control shall accelerate and become vested under the applicable option agreements to the extent such stock options are outstanding and unexercisable at the time of such termination and all stock subject to a right of repurchase by the Company (or its successor) that was purchased prior to the Change of Control shall have such right of repurchase lapse (notwithstanding any provision to the contrary in a "Stock Vesting Agreement" dated November 24, 2004 between Employee and the Company);

(3) the Employee shall be permitted to exercise all vested (including shares that vest as a result of this Agreement) stock options granted by the Company to the Employee prior to the Change of Control for a period of two (2) years following the Termination Date; and

(4) the same level of Company-paid health (i.e., medical, vision and dental) coverage and benefits for such coverage as in effect for the Employee (and any eligible dependents) on the day immediately preceding the Employee's Termination Date; provided, however, that (i) the Employee constitutes a qualified beneficiary, as defined in Section 4980B(g)(1) of the Internal Revenue Code of 1986, as amended; and (ii) Employee elects continuation coverage pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), within the time period prescribed pursuant to COBRA. The Company shall continue to provide Employee with such Company-paid coverage until the earlier

of (i) the date Employee (and his/her eligible dependents) is no longer eligible to receive continuation coverage pursuant to COBRA, or (ii) twelve (12) months from the Termination Date.

(b) Termination of Clinical or Scientific Advisory Board Service Following a Change of Control If the Employee has terminated his employment with the company but remains a participant on the Company's Clinical or Scientific Advisory Board at the time of a Change of Control and his participation is terminated by the Company without Cause at any time within eighteen (18) months after a Change of Control and the Employee signs the release of claims pursuant to Section 7 hereto, Employee shall be entitled to the following severance benefits:

(1) all stock options granted by the Company to the Employee prior to the Change of Control shall accelerate and become vested under the applicable option agreements to the extent such stock options are outstanding and unexercisable at the time of such termination and all stock subject to a right of repurchase by the Company (or its successor) that was purchased prior to the Change of Control shall have such right of repurchase lapse (notwithstanding any provision to the contrary in the Stock Vesting Agreement) and

(2) the Employee shall be permitted to exercise all vested (including shares that vest as a result of this Agreement) stock options granted by the Company to the Employee prior to the Change of Control for a period of two (2) years following the Termination Date.

(c) Termination Apart from a Change of Control. If (but without duplication with the provisions set forth above in subsection 4(a) or 4(b)) the Employee's employment with the Company terminates as a result of an Involuntary Termination, the Employee shall be entitled to severance benefits in the form of twelve (12) months of Employee's base salary as in effect as of the date of termination, less applicable withholding, payable in a lump sum within thirty (30) days of the Involuntary Termination.

(d) Accrued Wages and Vacation, Expenses. Without regard to the reason for, or the timing of, Employee's termination of employment: (i) the Company shall pay the Employee any unpaid base salary due for periods prior to the Termination Date; (ii) the Company shall pay the Employee all of the Employee's accrued and unused vacation through the Termination Date; and (iii) following submission of proper expense reports by the Employee, the Company shall reimburse the Employee for all expenses reasonably and necessarily incurred by the Employee in connection with the business of the Company prior to the Termination Date. These payments shall be made promptly upon termination and within the period of time mandated by law.

5. Limitation on Payments. In the event that the severance and other benefits provided for in this Agreement or otherwise payable to the Employee (i) constitute "parachute payments" within the meaning of Section 280G of the Code, and (ii) would be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then Employee's benefits under this Agreement shall be either

(a) delivered in full, or

(b) delivered as to such lesser extent which would result in no portion of such benefits being subject to the Excise Tax,

whichever of the foregoing amounts, taking into account the applicable federal, state and local income taxes and the Excise Tax, results in the receipt by Employee on an after-tax basis, of the greatest amount of benefits, notwithstanding that all or some portion of such benefits may be taxable under Section 4999 of the Code.

Unless the Company and the Employee otherwise agree in writing, any determination required under this Section shall be made in writing by the Company's independent public accountants (the "Accountants"), whose determination shall be conclusive and binding upon the Employee and the Company for all purposes. For purposes of making the calculations required by this Section, the Accountants may make reasonable assumptions and approximations concerning applicable taxes and may rely on reasonable, good faith interpretations concerning the application of Section 280G and 4999 of the Code. The Company and the Employee shall furnish to the Accountants such information and documents as the Accountants may reasonably request in order to make a determination under this Section. The Company shall bear all costs the Accountants may reasonably incur in connection with any calculations contemplated by this Section.

6. Successors.

(a) Company's Successors. Any successor to the Company (whether direct or indirect and whether by purchase, lease, merger, consolidation, liquidation or otherwise) to all or substantially all of the Company's business and/or assets shall assume the Company's obligations under this Agreement and agree expressly to perform the Company's obligations under this Agreement in the same manner and to the same extent as the Company would be required to perform such obligations in the absence of a succession. For all purposes under this Agreement, the term "Company" shall include any successor to the Company's business and/or assets which executes and delivers the assumption agreement described in this subsection (a) or which becomes bound by the terms of this Agreement by operation of law.

(b) Employee's Successors. Without the written consent of the Company, Employee shall not assign or transfer this Agreement or any right or obligation under this Agreement to any other person or entity. Notwithstanding the foregoing, the terms of this Agreement and all rights of Employee hereunder shall inure to the benefit of, and be enforceable by, Employee's personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees.

7. Execution of Release Agreement upon Termination. As a condition of entering into this Agreement and receiving the benefits under Section 4, the Employee agrees to execute and not revoke a general release of claims upon the termination of employment with the Company, and to execute and not revoke a general release of claims upon the termination of participation as a clinical or scientific advisor with the Company.

8. Notices.

(a) General. Notices and all other communications contemplated by this Agreement shall be in writing and shall be deemed to have been duly given when personally delivered or when mailed by U.S. registered or certified mail, return receipt requested and postage prepaid. In the case of the Employee, mailed notices shall be addressed to Employee at the home address which Employee most recently communicated to the Company in writing. In the case of the Company, mailed notices shall be addressed to its corporate headquarters, and all notices shall be directed to the attention of its Chief Executive Officer.

(b) Notice of Termination. Any termination by the Company for Cause or by the Employee as a result of a voluntary resignation shall be communicated by a notice of termination to the other party hereto given in accordance with this Section. Such notice shall indicate the specific termination provision in this Agreement relied upon, shall set forth in reasonable detail the facts and circumstances claimed to provide a basis for termination under the provision so indicated, and shall specify the Termination Date (which shall be not more than 30 days after the giving of such notice). The failure by the Employee to provide the notice or to include in the notice any fact or circumstance which contributes to a showing of Involuntary Termination shall not waive any right of the Employee hereunder or preclude the Employee from asserting such fact or circumstance in enforcing his rights hereunder.

9. Arbitration.

(a) Any dispute or controversy arising out of, relating to, or in connection with this Agreement, or the interpretation, validity, construction, performance, breach, or termination thereof, shall be settled by binding arbitration to be held in Santa Clara, California, in accordance with the National Rules for the Resolution of Employment Disputes then in effect of the American Arbitration Association (the "Rules"). The arbitrator may grant injunctions or other relief in such dispute or controversy. The decision of the arbitrator shall be final, conclusive and binding on the parties to the arbitration. Judgment may be entered on the arbitrator's decision in any court having jurisdiction. The arbitrator may require one party to pay the costs and attorney fees of the prevailing party.

(b) The arbitrator(s) shall apply California law to the merits of any dispute or claim, without reference to conflicts of law rules. The arbitration proceedings shall be governed by federal arbitration law and by the Rules, without reference to state arbitration law. Employee hereby consents to the personal jurisdiction of the state and federal courts located in California for any action or proceeding arising from or relating to this Agreement or relating to any arbitration in which the parties are participants.

(c) Employee understands that nothing in this Section modifies Employee's at-will employment status. Either Employee or the Company can terminate the employment relationship at any time, with or without Cause.

(d) EMPLOYEE HAS READ AND UNDERSTANDS THIS SECTION, WHICH DISCUSSES ARBITRATION. EMPLOYEE UNDERSTANDS THAT SUBMITTING ANY CLAIMS ARISING OUT OF, RELATING TO, OR IN CONNECTION WITH THIS AGREEMENT, OR THE INTERPRETATION, VALIDITY, CONSTRUCTION, PERFORMANCE, BREACH OR TERMINATION THEREOF TO BINDING ARBITRATION, CONSTITUTES A WAIVER OF EMPLOYEE'S RIGHT TO A JURY TRIAL AND RELATES TO THE RESOLUTION OF ALL DISPUTES RELATING TO ALL ASPECTS OF THE EMPLOYER/EMPLOYEE RELATIONSHIP, INCLUDING BUT NOT LIMITED TO, THE FOLLOWING CLAIMS:

(i) ANY AND ALL CLAIMS FOR WRONGFUL DISCHARGE OF EMPLOYMENT; BREACH OF CONTRACT, BOTH EXPRESS AND IMPLIED; BREACH OF THE COVENANT OF GOOD FAITH AND FAIR DEALING, BOTH EXPRESS AND IMPLIED; NEGLIGENT OR INTENTIONAL INFLICTION OF EMOTIONAL DISTRESS; NEGLIGENT OR INTENTIONAL MISREPRESENTATION; NEGLIGENT OR INTENTIONAL INTERFERENCE WITH CONTRACT OR PROSPECTIVE ECONOMIC ADVANTAGE; AND DEFAMATION.

(ii) ANY AND ALL CLAIMS FOR VIOLATION OF ANY FEDERAL STATE OR MUNICIPAL STATUTE, INCLUDING, BUT NOT LIMITED TO, TITLE VII OF THE CIVIL RIGHTS ACT OF 1964, THE CIVIL RIGHTS ACT OF 1991, 1 AGE DISCRIMINATION IN EMPLOYMENT ACT OF 1967, THE AMERICANS WITH DISABILITIES ACT OF 1990, THE FAIR LABOR STANDARDS ACT, THE CALIFORNIA FAIR EMPLOYMENT AND HOUSING ACT, AND LABOR CODE SECTION 20 1, *et seq*;

(iii) ANY AND ALL CLAIMS ARISING OUT OF ANY OTHER LAWS AND REGULATIONS RELATING TO EMPLOYMENT OR EMPLOYMENT DISCRIMINATION.

10. Miscellaneous Provisions.

(a) Effect of Statutory Benefits. To the extent that any severance benefits are required to be paid to the Employee upon termination of employment with the Company as a result of any requirement of law or any governmental entity in any applicable jurisdiction, the aggregate amount of severance benefits payable pursuant to Section 4 hereof shall be reduced by such amount.

(b) No Duty to Mitigate. The Employee shall not be required to mitigate the amount of any payment contemplated by this Agreement, nor shall any such payment be reduced by any earnings that the Employee may receive from any other source.

(c) Waiver. No provision of this Agreement may be modified, waived or discharged unless the modification, waiver or discharge is agreed to in writing and signed by the Employee and by an authorized officer of the Company (other than the Employee). No waiver by

either party of any breach of, or of compliance with, any condition or provision of this Agreement by the other party shall be considered a waiver of any other condition or provision or of the same condition or provision at another time.

(d) Integration. This Agreement, the Stock Vesting Agreement and any outstanding stock option agreements and any restricted stock purchase agreements referenced herein or therein represent the entire agreement and understanding between the parties as to the subject matter herein and supersede all prior or contemporaneous agreements, whether written or oral, with respect to this Agreement and any stock option agreement or any restricted stock purchase agreement, provided, that, for clarification purposes, this agreement shall not affect any agreements between the Company and Employee regarding intellectual property matters or confidential information of the Company.

(e) Choice of Law. The validity, interpretation, construction and performance of this Agreement shall be governed by the internal substantive laws, but not the conflicts of law rules, of the State of California.

(f) Severability. The invalidity or unenforceability of any provision or provisions of this Agreement shall not affect the validity or enforceability of any other provision hereof, which shall remain in full force and effect.

(g) Employment Taxes. All payments made pursuant to this Agreement shall be subject to withholding of applicable income and employment taxes.

(h) Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together will constitute one and the same instrument.

IN WITNESS WHEREOF, each of the parties has executed this Agreement, in the case of the Company by its duly authorized officer, as of the day and year first above written.

COMPANY:

Threshold Pharmaceuticals, Inc.

By: /s/ Harold E. Selick

Title: Chief Executive Officer

EMPLOYEE:

/s/ George F. Tidmarsh

Signature

George F. Tidmarsh

Printed Name

THRESHOLD PHARMACEUTICALS, INC
STOCK VESTING AGREEMENT

This Stock Vesting Agreement (the "Agreement") is entered into effective December 23, 2004, between Threshold Pharmaceuticals, Inc. ("Threshold" or the "Company") and George F. Tidmarsh, M.D., Ph.D. ("Tidmarsh").

RECITALS

A. Tidmarsh is a founder of Threshold and currently serves as the Company's President and as a member of the Company's Board of Directors.

B. Tidmarsh has acquired or may acquire the following shares of the Company's Common Stock: (1) 250,000 shares (after giving effect to a 1:10 reverse split) acquired pursuant to a Founder Stock Purchase Agreement dated October 24, 2001 (the "Founder Shares"); (2) 882,500 shares acquired on April 20, 2004, upon exercise of an option granted on August 6, 2002 (the "August 2002 Shares"); (3) 525,000 shares acquired on April 20, 2004, upon exercise of an option granted on March 10, 2004 (the "March 2004 Shares"); and (4) 200,000 shares Tidmarsh may acquire, upon exercise of an option granted on May 12, 2004 (the "May 2004 Shares") and together with the Founder Shares, August 2002 Shares and March 2004 Shares, the "Shares").

C. All of the Shares are subject to a repurchase right by the Company that lapses according to schedules and conditions set forth in the respective agreements or grant notices with respect to such shares (the "Share Agreements"). As of December 31, 2005, provided that the conditions for the release of shares from the Company's repurchase right set forth in the respective Share Agreements shall have been satisfied, the repurchase right shall have lapsed with respect to 199,350 of the Founder Shares, 703,706 of the August 2002 Shares, 229,320 of the March 2004 Shares and 79,162 of the May 2004 Shares.

D. Threshold and Tidmarsh each acknowledge Tidmarsh's contributions to the Company and desire to enter into this Agreement to provide additional incentives for Tidmarsh to complete certain activities and continue full time employment with the Company until at least December 31, 2005.

Now therefore in consideration of the covenants set forth below, and for good and valuable consideration receipt of which is hereby acknowledged, the parties agree as follows:

AGREEMENT

1. **Acceleration of Vesting for Full-Time Employment Through December 31, 2005** Notwithstanding anything to the contrary set forth in any of the Share Agreements, in the event that (a) (x) Tidmarsh remains a full-time employee of the Company until December 31, 2005, and (y) as of such date the activities set forth on Exhibit A shall have been completed by or under the supervision of Tidmarsh to the satisfaction of the Company's Chief Executive Officer, or (b) prior to December 31, 2005, Tidmarsh suffers an Involuntary Termination as defined in his Change of Control Severance Agreement with the Company, then:

(i) effective as of December 31, 2005 (or as of the date of termination with respect to (b) above), the Company's repurchase right with respect to all of the Founder Shares, the August 2002 shares and the May 2004 Shares shall terminate in its entirety, and the Company shall no longer have any right to repurchase such shares.

(ii) after December 31, 2005, the Company's repurchase right shall continue to lapse with respect to the March 2004 Shares according to the schedule set forth in the respective Share Agreement, provided that Continuous Service shall be deemed to include membership in good standing on the Company's Scientific or Clinical Advisory Board.

2. **No Guarantee of Employment.** This Agreement is not to be interpreted as a guarantee or contract of continuing employment. Tidmarsh's employment remains "at will" notwithstanding anything in this Agreement. The Company agrees that if Tidmarsh's full-time employment with the Company terminates, and Tidmarsh has performed satisfactorily as determined by the Company's Chief Executive Officer, he will be given the opportunity to participate as a member of the Company's Clinical or Scientific Advisory Board.

3. **No Other Amendments.** Except as expressly provided herein, the Share Agreements shall remain in full force and effect according to their respective terms.

4. **Miscellaneous.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original and all of which together shall constitute one instrument. The benefits and obligations of this Agreement will be binding on the executors, administrators, heirs, legal representatives, successors, and assigns of the parties. This Agreement shall be governed by, and construed in accordance with, the laws of the State of California excluding those laws that direct the application of the laws of another jurisdiction.

[Signature Page Follows]

The parties have executed this Agreement effective as of the first date written above.

THRESHOLD PHARMACEUTICALS, INC.

By: /s/ Harold E. Selick

Title: Chief Executive Officer

/s/ George F. Tidmarsh

George F. Tidmarsh, M.D., Ph.D.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the use in this Amendment No. 4 to Registration Statement on Form S-1 of our report dated April 8, 2004, relating to the financial statements of Threshold Pharmaceuticals, Inc., which appears in such Registration Statement. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PRICEWATERHOUSECOOPERS LLP

San Jose, California
December 28, 2004