As filed with the Securities and Exchange Commission on January 28, 2005

Registration No. 333-114376

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

AMENDMENT NO. 6 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)

Delaware	**2834**	**94-3409596**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification No.)**

Harold E. Selick, Ph.D.
Chief Executive Officer
1300 Seaport Boulevard
Redwood City, California 94063
Telephone: (650) 474-8200
Facsimile: (650) 474-2529
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Sarah A. O'Dowd
Stephen B. Thau
Heller Ehrman White & McAuliffe LLP
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

Danielle Carbone
Shearman & Sterling LLP
599 Lexington Avenue
New York, New York 10022
Telephone: (212) 848-4000
Facsimile: (212) 848-7179

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	$98,133,328	$12,327

(1) 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.

Table of Contents

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 JANUARY 28, 2005

THRESHOLD PHARMACEUTICALS, INC.

COMMON STOCK

Threshold Pharmaceuticals, Inc. is offering 5,333,333 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 $14.00 and $16.00 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 8.

	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 800,000 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

TABLE OF CONTENTS

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 is being evaluated in a Phase 2 clinical trial. We have completed enrollment in this trial, and we are evaluating interim data. Interim data are preliminary results from a predetermined portion of study participants. 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 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 being evaluated 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 interim data. We observed statistically significant improvements in all variables measured 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. Our registrational program will include multiple multi-center, randomized, double-blinded, placebo-controlled studies, including at least one dose-comparison study. We expect to commence two clinical trials in the first half of 2005, one of which we believe will be a Phase 3 trial. There can be no assurance that regulatory agencies will consider this Phase 3 trial pivotal. Our registrational program will 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.

THE OFFERING

Common stock offered	5,333,333 shares
Common stock to be outstanding after the offering	29,254,907 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 3,368,759 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 20,552,815 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:

- 265,338 shares of our common stock that were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 256,979 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2004 at a weighted average exercise price of $0.39 per share;
- 23,073 shares of common stock issuable upon exercise of a warrant outstanding as of September 30, 2004 with an exercise price of $1.65 per share, which does not expire upon the closing of this offering;
- 533,903 shares of common stock available for future grants under our 2001 Equity Incentive Plan as of September 30, 2004;
- 2,428,805 shares of common stock reserved for issuance under our 2004 Equity Incentive Plan; and
- 750,000 shares of common stock reserved for issuance under our 2004 Employee Stock Purchase Plan.

Unless otherwise indicated, all information in this prospectus (i) assumes that the underwriters do not exercise their option to purchase up to 800,000 shares of our common stock to cover over-allotments, if any, (ii) assumes 20,552,815 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 and (iii) gives effect to a 1 for 1.6469 reverse stock split of our common stock effected on January 26, 2005.

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	$ (2.13)	$ (34.62)	$ (501.68)	$ (67.35)	$ (26.57)	
Weighted average number of shares used in per common share calculations:						
Basic and diluted	111	71	98	96	591	
Pro forma net loss per common share (unaudited):						
Basic and diluted[(1)]			$ (6.66)		$ (0.74)	
Weighted average number of shares used in pro forma per common share calculations (unaudited):						
Basic and diluted			7,381		21,144	

(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 20,552,815 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.

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 20,552,815 shares of our common stock upon the completion 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 $15.00 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	$ 88,752
Working capital	28,587	28,587	101,102
Total assets	31,375	31,375	103,890
Notes payable, less current portion	185	185	185
Redeemable convertible preferred stock	49,839	—	—
Total stockholders' equity (deficit)	(20,940)	28,899	101,414

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, and our registrational program will include additional 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.

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.

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 as a male contraceptive and is known to cause reversible effects on fertility in animals. In human clinical trials at doses significantly higher than the dose of TH-070 we contemplate investigating for BPH, muscle and testicular pain have been observed. 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

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

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;

- 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

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 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

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.

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;

- 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.

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

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

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-flurouracil, or 5-FU, a generic product which is sold by many manufacturers. In addition, Camptosar®, marketed by Pfizer, and Taxotere, marketed by the sanofi-aventis Group, 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. 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.

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.

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, or 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 Environmental Protection Agency, or 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.

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;

- 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 our 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 $11.53 in net tangible book value per share of common stock, based on an assumed initial public offering price of $15.00 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 72% 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

subject to a 180-day lock-up on the sale of their shares. After the lock-up expires, at least 5,333,333 shares of our common stock will become freely tradeable, 20,731,505 shares of common stock will be tradeable subject to Rule 144 and holders of 20,552,815 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 5,333,333 shares of common stock in this offering will be approximately $72.5 million, assuming an initial public offering price of $15.00 per share, the midpoint 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 $11.2 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.

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 20,552,815 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 5,333,333 shares of common stock by us in this offering at an assumed initial public offering price of $15.00 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	$ 88,752
Notes payable, less current portion	$ 185	$ 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, $0.001 par value per share; no shares authorized, actual and pro forma, and no 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; 30,360,070 shares authorized, actual, pro forma, and pro forma as adjusted; and 3,368,759 shares issued and outstanding, actual; 23,921,574 shares issued and outstanding, pro forma; and 29,254,907 shares issued and outstanding pro forma as adjusted	3	24	29
Additional paid-in capital	21,903	71,721	144,231
Deferred stock-based compensation	(16,244)	(16,244)	(16,244)
Accumulated other comprehensive income	98	98	98
Deficit accumulated during the development stage	(26,700)	(26,700)	(26,700)
Total stockholders' equity (deficit)	(20,940)	28,899	101,414
Total capitalization	$ 29,084	$ 29,084	$ 101,599

The table above excludes:

- 265,338 shares of our common stock that were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 256,979 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2004 at a weighted average exercise price of $0.39 per share;
- 38,000 shares of preferred stock issuable upon exercise of a warrant outstanding as of September 30, 2004 at an exercise price of $1.00 per share (convertible into 23,073 shares of common stock at an exercise price of $1.65 per share after giving effect to a 1 for 1.6469 reverse stock split effected January 26, 2005), which does not expire upon the closing of this offering;
- 533,903 shares of common stock available for future grants under our 2001 Equity Incentive Plan as of September 30, 2004;
- 2,428,805 shares of common stock reserved for issuance under our 2004 Equity Incentive Plan; and
- 750,000 shares of common stock reserved for issuance under our 2004 Employee Stock Purchase Plan.

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 $(6.22) per share of common stock. Pro forma net tangible book value as of September 30, 2004 was approximately $28.9 million or $1.21 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 20,552,815 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 5,333,333 shares of common stock offered by this prospectus, assuming an initial public offering price of $15.00 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 September 30, 2004 would have been approximately $101.4 million, or $3.47 per share. This represents an immediate increase in the pro forma net tangible book value of $2.26 per share to existing stockholders and an immediate dilution of $11.53 per share to new investors. This dilution is illustrated by the following table:

Assumed initial public offering price per share		$15.00
Historical net tangible book value per share as of September 30, 2004	(6.22)	
Increase per share due to assumed conversion of all shares of convertible preferred stock	7.43	
Pro forma net tangible book value per share before this offering	$ 1.21	
Increase per share attributable to this offering	2.26	
Pro forma as adjusted net tangible book value per share after the offering		3.47
Dilution per share to new investors		$11.53

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 20,552,815 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 $15.00 per share before deducting underwriting discounts and commissions and estimated offering costs payable by us:

	Total Shares		Total Consideration		
	Number	%	Amount	%	Average Price Per Share
Existing stockholders	23,921,574	81.8	$ 50,712,000	38.8	$ 2.12
New investors	5,333,333	18.2	$ 80,000,000	61.2	$ 15.00
Totals	29,254,907	100.0	$ 130,712,000	100.0	$ 4.47

The foregoing discussion and tables exclude:

- 265,338 shares of our common stock that were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 256,979 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2004 at a weighted average exercise price of $0.39 per share;
- 23,073 shares of common stock issuable upon conversion of preferred stock issuable upon exercise of a warrant outstanding as of September 30, 2004 with an exercise price of $1.65 per share, which does not expire upon the closing of this offering;

- 533,903 shares of common stock available for future grants under our 2001 Equity Incentive Plan as of September 30, 2004;
- 2,428,805 shares of common stock reserved for issuance under our 2004 Equity Incentive Plan; and
- 750,000 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 79.6% 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 6,133,333, or approximately 20.4% of the total pro forma as-adjusted number of shares of our common stock outstanding after this offering.

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, 2002	Years Ended December 31, 2003	Nine Months Ended September 30, 2003	Nine Months Ended September 30, 2004	Cumulative Period from October 17, 2001 (date of inception) to September 30, 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	$ (2.13)	$(34.62)	$(501.68)	$(67.35)	$ (26.57)	
Weighted average number of shares used in per common share calculations:						
Basic and diluted	111	71	98	96	591	
Pro forma net loss per common share (unaudited) (see Note 13):						
Basic and diluted			$ (6.66)		$ (0.74)	
Weighted average number of shares used in pro forma per common share calculations (unaudited) (see Note 13):						
Basic and diluted			7,381		21,144	

	As of December 31, 2001	As of December 31, 2002	As of December 31, 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	(234)	(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.

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, we granted options to purchase 386,778 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

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 million 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 our 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

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 our 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

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

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.

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 (convertible into 23,073 shares of common stock after giving effect to a 1 for 1.6469 reverse stock split effected January 26, 2005) 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 expired on December 31, 2004.

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

	Within one year	One to three years	Four to five years	After five years	Total
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., together Baxter, 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

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 $0.16 to $0.53 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 $0.16 to $16.38 per share during that period.

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

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.

In December 2004, the FASB issued SFAS No. 123 (revised 2004) ("SFAS No. 123(R)"),*"Share-Based Payment."* SFAS No. 123(R) requires all share-based payments to employees, including grants of employee stock options, to be recognized in the financial statements based on their fair values and is effective for public companies for interim or annual periods beginning after June 15, 2005. We are analyzing our options for the adoption of SFAS No. 123(R), which is effective as of July 1, 2005.

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

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

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.

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

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

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 up to 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 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 1.6 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 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.

	Changes from Baseline			
	Prostate Size	Maximum Urine Flow Rate	IPSS (units)	PSA
Day 14	– 6.5%	+3.1 mL/sec	not determined	– 1.5%
Day 28	–11.1%	+3.2 mL/sec	–7.3	–17.8%

In particular, at day 28 of treatment the average decrease in prostate size was 5.9 cc (–11.2%), the average increase in maximum urine flow rate was 3.2 mL/sec. (an increase from 9.4 mL/sec to 12.6 mL/sec), and the

average decrease in PSA levels was 0.7 ng/mL (–17.8%). TH-070 was well tolerated with no therapy-related side effects. These observations are based on interim data, and 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, as well as to confirm the absence of latent adverse effects.

We expect to publish 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, one of which we believe will be a Phase 3 trial. There can be no assurance that regulatory authorities will consider this Phase 3 trial pivotal. Our registrational program will 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 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 clinical trials for the treatment of symptomatic BPH in the first half of 2005, one of which we believe will be a Phase 3 trial. 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

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.

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.

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, 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. In connection with the Development Agreement, we granted to MediBIC a non-exclusive license to use Threshold confidential information relating to glufosfamide for the limited purpose of preparing the development plan and any associated marketing plans as authorized under the Development Agreement, and if the development plan is agreed upon, a non-exclusive license to use Threshold confidential information for the time necessary for MediBIC to perform its obligations under the development plan.

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

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 Drs. Lampidis and 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 Drs. Lampidis and 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.

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

with novel mechanisms of action. Our glufosfamide product candidate for pancreatic cancer will compete with Gemzar, marketed by Lilly, and 5-flurouracil, 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 the sanofi-aventis Group, 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. 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;

- 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, or 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

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.

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, or 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.

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, or 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.

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)
Executive Officers and Directors		
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
Alan Colowick	42	Chief Medical Officer
Wilfred E. Jaeger, M.D.[1][2]	48	Director
Michael F. Powell, Ph.D.[1]	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
Significant Employee		
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.

Alan Colowick, M.D., M.P.H has served as our Chief Medical Officer since January 2005. From 1999 to 2005, Dr. Colowick held a variety of positions with Amgen, most recently as Vice President of European

Medical Affairs. Prior to that, Dr. Colowick worked as senior director of medical affairs and director of product development. Dr. Colowick received his M.D. from the Stanford University School of Medicine and his M.P.H from the Harvard School of Public Health. He completed sub-specialty training in hematology and oncology at Brigham and Women's Hospital and the Dana Farber Cancer Institute.

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 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 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 our scientific and clinical advisors:

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.

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) and Dr. Wilfred E. Jaeger. 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 our common stock 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.

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 and 2004 by our chief executive officer and our other executive officers who were serving as executive officers on such dates and whose salary and bonus exceeded $100,000 for services rendered to us in all capacities during the year ended December 31, 2003 or 2004.

		Annual Compensation		Long Term Compensation
Name And Principal Position(s)	Year	Salary	Bonus	Securities Underlying Options
Harold E. Selick, Ph.D.(1)	2004	$ 295,833	$ 274,614	576,841
Chief Executive Officer	2003	169,007	—	464,252
George F. Tidmarsh, M.D., Ph.D.(2)	2004	245,833	236,250	440,221
Founder and President	2003	200,000	—	—
Janet I. Swearson(3)	2004	217,083	91,375	245,916
Chief Financial Officer	2003	238,500	—	97,152

(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 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.

(2) As of February 1, 2004, Dr. Tidmarsh's annual compensation was increased to $250,000.

(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.

Option Grants In Year Ended December 31, 2004. The following table sets forth each grant of stock options during the fiscal year ended December 31, 2004 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 2,062,663 shares of common stock granted by us during the fiscal year ended December 31, 2004 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 $15.00 (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	445,401(1)	22.08%	$ 0.26	3/9/2014	$ 10,931,536	$ 17,406,645
	121,440(2)	5.89%	0.53	5/11/2014	2,862,945	4,558,762
George F. Tidmarsh, M.D., Ph.D	318,781(1)	15.45%	0.26	3/9/2014	7,652,083	12,184,663
	121,440(2)	5.89%	0.53	5/11/2014	2,862,945	4,558,762
Janet I. Swearson	209,484(1)	10.16%	0.26	3/9/2014	5,028,496	8,007,039
	36,432(2)	1.77%	0.53	5/11/2014	858,884	1,367,629

(1) Stock options vest in equal monthly installments over four years from the vesting commencement date.
(2) Stock options vest 25% as of the one-year anniversary of the grant date with the remaining shares vesting in equal monthly installments over the following 36 months.

Aggregated Option Exercises During Year Ended December 31, 2004 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, 2004. There was no public trading market for our common stock as of December 31, 2004. 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 $15.00 per share, which is the midpoint of the range listed on the cover of this prospectus.

Named executive officers	Number of Shares Acquired	Value Realized(1)	Number of Securities Underlying Unexercised Options at December 31, 2004		Value of Unexercised In-The-Money Options at December 31, 2004	
			Exercisable(2)	Unexercisable	Exercisable	Unexercisable
Harold E. Selick, Ph.D.	1,127,050	$16,634,949	—	—	$ —	—
George F. Tidmarsh, M.D., Ph.D	854,636	12,650,920	121,440	—	1,757,237	—
Janet I. Swearson	348,988	5,144,554	—	—	—	—

(1) These values have been calculated based on an assumed initial public offering price of $15.00, the midpoint of the range on the cover of this prospectus, less the applicable exercise price per share, multiplied by the underlying shares, without taking into account any taxes that may be payable in connection with the transaction.
(2) The outstanding option may be exercised at any time, whether vested or unvested. Upon the exercise of an unvested option or the unvested portion of an option, the holder will receive shares of restricted stock that are subject to our repurchase right at the original purchase price of the shares, which repurchase right lapses in accordance with the vesting schedule previously applicable to the option.

Change of Control Severance Agreements

In December 2004, we entered into change of control severance agreements with Dr. Selick, Ms. Swearson and Dr. Matteucci, and in January 2005, we entered into a similar agreement with Dr. Colowick. 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 216,484 shares of common stock held by Dr. Tidmarsh will terminate, and the vesting of options to purchase up to 121,440 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 259,009 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 4,250,409 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.

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:

- 265,338 shares were issued upon the exercise of options at a purchase price of $0.53 per share, but were subject to a call feature as of September 30, 2004, which call feature has since been cancelled;
- 256,979 shares were issuable upon exercise of outstanding options granted under this plan at a weighted average exercise price of $0.39 per share;
- 1,675,207 shares were issued upon exercise of options at a purchase price of $0.16 per share, 1,408,777 shares were issued upon exercise of options at a purchase price of $0.26 per share, and 110,205 shares were issued upon exercise of options at a purchase price of $0.53 per share; and
- 533,903 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, (i) give effect to a 1 for 1.6469 reverse stock split of our common stock effected January 26, 2005 and (ii) 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 in the future. Upon the completion 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 or directors.

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 2,428,805 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 us 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 of directors 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.

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) 1,214,402 shares and (c) a number of shares set by our board of directors.

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 18,216 shares of our common stock upon their initial appointment to our board of directors, 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 6,072 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.

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 us 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 of directors adopted the 2004 Employee Stock Purchase Plan, or 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 750,000 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;
- 500,000 shares; or
- a lesser number as determined by the Compensation Committee of our board of directors prior to such January 1.

Administration. The Compensation Committee appointed by our board of directors, 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, 2007 and the initial purchase period will end August 15, 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 our board of directors, but excludes all other payments including long-term disability or workers' compensation payments, car allowances, relocation payments and expense reimbursements.

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. Our board of directors 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 approximately 0.6072 shares 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 5,920 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.

Our Senior Director of Investor Relations, Denise Powell, a Threshold employee, is the sister of Michael Powell, a member of our Board of Directors and a member of the audit committee. Ms. Powell's annualized salary is $140,000. She may also be eligible for additional bonuses. In addition, in January 2005, Ms. Powell was granted an option to purchase 45,540 shares of our common stock. Twenty-five percent of these shares vest on the one-year anniversary of the commencement of Ms. Powell's employment with us, and the remaining shares vest monthly over the subsequent three years. Prior to becoming an employee of Threshold in January 2005, Ms. Powell was an independent investor relations consultant. From 1992 to 1998, Ms. Powell held a variety of positions at Amgen, including Associate Director of Investor Relations from 1995 to 1998.

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 23,921,574 shares of common stock outstanding as of September 30, 2004 assuming (i) the conversion of all of our outstanding convertible preferred stock and shares of common stock immediately outstanding after completion of this offering and (ii) gives effect to a 1 for 1.6469 reverse stock split of our common stock effected January 26, 2005. Unless otherwise noted below, the address of each person listed on the table is c/o Threshold Pharmaceuticals, Inc., 1300 Seaport Boulevard, Redwood City, CA 94063.

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	3,312,007	13.8%	11.3%
Pequot Capital Management, Inc.[2] 500 Nyala Farm Road Westport, CT 06880	3,312,006	13.8%	11.3%
Entities affiliated with ProQuest Investments[3] 12626 High Bluff Drive Suite 360 San Diego, California 92130	3,206,205	13.4%	10.9%
Entities affiliated with Sofinnova Ventures, Inc.[4] 140 Geary Street Tenth Floor San Francisco, CA 94108	3,206,202	13.4%	10.9%
Entities affiliated with Three Arch Partners[5] 3200 Alpine Road Portola Valley, CA 94028	3,206,204	13.4%	10.9%
Entities affiliated with Sutter Hill Ventures[6] 755 Page Mill Road, Suite A-200 Palo Alto, CA 94304-1005	2,264,406	9.4%	7.7%

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]	1,127,049	4.7%	3.8%
George F. Tidmarsh, M.D., Ph.D.[8]	1,127,875	4.7%	3.8%
Janet I. Swearson[9]	348,988	1.4%	1.1%
Ralph E. Christoffersen[10]	3,312,007	13.8%	11.3%
Patrick G. Enright[11]	3,312,006	13.8%	11.3%
Wilfred E. Jaeger[12]	3,206,204	13.4%	10.9%
Michael F. Powell[13]	3,206,202	13.4%	10.9%
William A. Halter[14]	—		
George G.C. Parker[15]	—		
All directors and executive officers as a group (9 persons)[16]	15,640,331	65.4%	53.1%

(1) Includes 3,312,007 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 2,902,805 shares, and Pequot Offshore Private Equity Partners III, L.P., the holder of record of 409,201 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 3,076,996 shares held of record ProQuest Investments II, L.P. and 129,209 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 3,058,674 shares of record held by Sofinnova Venture Partners V, LP, 100,630 shares of record held by Sofinnova Venture Affiliates V, LP, and 46,898 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 3,042,652 shares of record held by Three Arch Partners III, L.P. and 163,552 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 22,146 shares held by Sutter Hill Entrepreneurs Fund (AI), L.P.; 56,077 shares held by Sutter Hill Entrepreneurs Fund (QP), L.P.; 2,186,183 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

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 684,708 shares which we have the right to repurchase as of the date that is 60 days after September 30, 2004.

(8) Includes 488,502 shares which we have the right to repurchase as of the date that is 60 days after September 30, 2004.

(9) Includes 261,603 shares which we have the right to repurchase as of the date that is 60 days after September 30, 2004.

(10) Includes 3,312,007 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 2,902,805 shares, and Pequot Offshore Private Equity Partners III, L.P., which may be deemed to be the holder of record of 409,201 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 3,206,204 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 3,206,202 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 36,432 shares to Mr. Halter, which options are exercisable within 60 days of September 30, 2004, of which 24,288 vest at the rate of $^{1}/_{36}$ per month commencing September 22, 2004 and 12,144 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 36,432 shares to Dr. Parker, which options are exercisable within 60 days of September 30, 2004, of which 24,288 vest at the rate of $^{1}/_{36}$ per month commencing September 22, 2004 and 12,144 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, 3,368,759 shares of common stock, 33,848,484 shares of preferred stock convertible into 20,552,815 shares of common stock upon the completion of this offering and a warrant to purchase 38,000 shares of preferred stock convertible into 23,073 shares of common stock upon completion of this offering were issued and outstanding. In addition, as of September 30, 2004, 265,338 shares of common stock were outstanding but subject to a call feature, which call feature has since been cancelled. The information presented herein regarding our common stock gives effect to a 1 for 1.6469 reverse stock split of our common stock effected January 26, 2005.
- 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 29,254,907 shares of common stock outstanding, assuming no exercise of the underwriters' over-allotment option and no exercise of options to acquire 256,979 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

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 Series A Preferred stock convertible into 23,073 shares of our common stock at an exercise price of $1.65 per share after giving effect to a 1 for 1.6469 reverse stock split effected January 26, 2005. 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 7,429,214 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 256,979 shares of common stock were issued and outstanding at a weighted average exercise price of $0.39 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 our common stock issued or issuable upon conversion of our outstanding preferred stock (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.

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 us 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 our board of directors 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

candidates for election as directors, other than nominations made by or at the direction of our 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 66⅔% of our then outstanding common stock, voting together as a single class.
- *Staggered Board of Directors.* 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 of directors, 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 66⅔% of our then outstanding common stock, voting together as a single class.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware. 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.

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 General Corporation Law of the State of Delaware 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 completion 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 the completion of this offering, 29,254,907 shares of common stock will be outstanding, assuming the issuance of an aggregate of 5,333,333 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 5,333,333 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 23,921,574 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 us 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 us, 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 us. Any person, or persons whose shares are aggregated, who is not deemed to have been an affiliate of us 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 us by our 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.

We have reserved an aggregate of 4,250,409 shares of common stock for issuance pursuant to our 2001 Equity Incentive Plan, of which options to purchase approximately 256,979 shares were outstanding as of September 30, 2004. We have also reserved an aggregate of 2,428,805 shares of common stock for issuance under our 2004 Equity Incentive Plan and 750,000 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 and CIBC World Markets Corp. 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 and CIBC World Markets Corp. in their 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 and CIBC World Markets Corp. 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 20,552,815 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.**

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

- 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.

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:

Underwriter	Number of Shares
Banc of America Securities LLC	
CIBC World Markets Corp.	
Lazard Frères & Co. LLC	
William Blair & Company, L.L.C	
Total	5,333,333

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 800,000 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.

	Paid by Threshold	
	No Exercise	Full Exercise
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

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.

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.

U.K. Selling Restrictions

Each underwriter has agreed that: (i) it has not offered or sold and, prior to the expiry of a period of six months from the closing date, will not offer or sell any shares of stock to persons in the United Kingdom except to persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of their businesses or otherwise in circumstances which have not resulted and will not result in an offer to the public in the United Kingdom within the meaning of the Public Offers of Securities Regulations 1995; (ii) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000, or FSMA) received by it in connection with the issue or sale of any shares of stock in circumstances in which section 21(1) of the FSMA does not apply to the issuer; and (iii) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of stock in, from or otherwise involving the United Kingdom.

No Public Offering Outside the United States

No action has been or will be taken in any jurisdiction (except in the United States) that would permit a public offering of our shares or the possession, circulation or distribution of this prospectus or any other material relating to us or our shares in any jurisdiction where action for that purpose is required. Accordingly, our shares may not be offered or sold, directly or indirectly, and neither this prospectus nor any other offering material or advertisements in connection with our shares may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Purchasers of the shares offered by this prospectus may be required to pay stamp taxes and other charges in accordance with the laws and practices of the country of purchase in addition to the offering price on the cover page of this 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.

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*.

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

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, except as to Note 12 which is as of January 26, 2005.

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

	December 31, 2002	December 31, 2003	September 30, 2004	Pro Forma Stockholders' Equity at September 30, 2004
			(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	
Total current assets	6,570	41,061	30,878	
Property and equipment, net	71	199	305	
Restricted cash	85	—	192	
Other assets	—	10	—	
Total assets	$ 6,726	$ 41,270	$ 31,375	
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	
Total current liabilities	416	884	2,291	
Notes payable, less current portion	—	242	185	
Total liabilities	416	1,126	2,476	
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	$ —
Stockholders' equity (deficit):				
Common stock, $0.001 par value:				
Authorized: 30,360,070 shares				
Issued and outstanding: 176,998 shares in 2002, 184,709 shares in 2003, 3,368,759 shares in 2004 (unaudited) and 23,921,574 shares pro forma (unaudited)	—	—	3	24
Additional paid-in-capital	52	2,685	21,903	71,721
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)
Total stockholders' equity (deficit)	(2,667)	(9,695)	(20,940)	$ 28,899
Total liabilities and stockholders' deficit	$ 6,726	$ 41,270	$ 31,375	

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

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	$ (2.13)	$(34.62)	$(501.68)	$(67.35)	$ (26.57)	
Weighted average number of shares used in per common share calculations:						
Basic and diluted	111	71	98	96	591	
Pro forma net loss per common share (unaudited)(see Note 13):						
Basic and diluted			$ (6.66)		$ (0.74)	
Weighted-average number of shares used in pro forma per common share calculations (unaudited)(see Note 13):						
Basic and diluted			7,381		21,144	

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

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 $0.02 per share	151,800	$ —	$ 2	$ —	$ —	$ —	$ 2
Net loss	—	—	—	—	—	(236)	(236)
Balances, December 31, 2001	151,800	—	2	—	—	(236)	(234)
Issuance of restricted common stock to a member of the Board of Directors for cash at $0.16 per share in January 2002	22,770	—	4	—	—	—	4
Issuance of common stock pursuant to exercise of stock options for cash at $0.16 per share	2,428	—	—	—	—	—	—
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	176,998	—	52	(24)	(1)	(2,694)	(2,667)
Issuance of common stock pursuant to exercise of stock options for cash at $0.16 per share	7,711	—	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	184,709	—	2,685	(1,546)	163	(10,997)	(9,695)
Issuance of common stock pursuant to exercise of stock options for cash at $0.16 per share (unaudited)	1,665,068	2	272	—	—	—	274
Issuance of common stock pursuant to exercise of stock options for cash at $0.26 per share (unaudited)	1,408,777	1	370	—	—	—	371
Issuance of common stock pursuant to exercise of stock options for cash at $0.53 per share (unaudited)	110,205	—	60	—	—	—	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)	3,368,759	$ 3	$ 21,903	$ (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, 2002	Years Ended December 31, 2003	Nine Months Ended September 31, 2003	Nine Months Ended September 31, 2004	Cumulative Period from October 17, 2001 (date of inception) to September 30, 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:						
Prepaids 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 20,552,815 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.

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,	
		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	136	174	183	182	1,960
Less: Weighted-average shares subject to repurchase	(25)	(103)	(85)	(86)	(1,369)
Weighted-average number of common shares outstanding used in computing basic and diluted net loss per common share	111	71	98	96	591

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	—	1,078	1,791	1,785	522
Common stock subject to repurchase	98	95	76	80	1,910
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

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	$ (2.13)	$(34.62)	$(501.68)	$(67.35)	$ (26.57)
Pro forma	$ (2.13)	$(34.79)	$(501.73)	$(67.41)	$ (24.75)

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 $0.05, $3.47 and $8.45 (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.

In December 2004, the FASB issued SFAS No. 123 (revised 2004) ("SFAS No. 123(R)"), "Share-Based Payment." SFAS No. 123(R) requires all share-based payments to employees, including grants of employee stock options, to be recognized in the financial statements based on their fair values and is effective for public companies for interim or annual periods beginning after June 15, 2005. The Company is analyzing its options for the adoption of SFAS No. 123(R), which is effective as of July 1, 2005.

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

NOTE 3—MARKETABLE SECURITIES:

	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
As of December 31, 2002 (in thousands):				
Common stock in a public company	$ 46	$ —	$ (1)	$ 45

	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
As of December 31, 2003 (in thousands):				
Common stock in a public company	$ 46	$ 163	$ —	$ 209

	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
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):

	December 31,	
	2002	2003
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):

	December 31,	
	2002	2003
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

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

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	$ 408

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	$ 2,535

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.

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

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 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 MediBIC, 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

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

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 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
	33,886,484	33,848,484	$ 49,839,000	

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

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

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.

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.

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

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 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. The per share conversion price of the Series A and B redeemable convertible preferred stock is $1.6469 and $2.7174, respectively (unaudited) after giving effect to the reverse stock split described in Note 12 to the financial statements.

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.

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

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.

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

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

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 95,367, 75,970 and 60,017 (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 Equity Incentive Plan (the "2001 Plan") under which the Company may issue incentive stock options and nonstatutory stock options. As of December 31, 2003, the Company has reserved 4,250,409 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 1,849,363 (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	1,214,402	—	$ —	$ —
Balances, December 31, 2001	1,214,402	—	—	—
Options granted	(1,080,024)	1,080,024	0.16	0.16
Options exercised	—	(2,428)	0.16	0.16
Balances, December 31, 2002	134,378	1,077,596	0.16	0.16
Additional shares reserved	3,036,007	—	—	—
Options granted	(726,564)	726,564	0.16–0.26	0.16
Options exercised	—	(7,711)	0.16	0.16
Options canceled	5,568	(5,568)	0.16	0.16
Balances, December 31, 2003	2,449,389	1,790,881	0.16–0.26	0.16
Options granted (unaudited)	(1,963,042)	1,963,042	0.26–0.53	0.33
Options exercised (unaudited)	—	(3,184,050)	0.16–0.53	0.22
Options canceled (unaudited)	47,556	(47,556)	0.16–0.53	0.18
Balances, September 30, 2004 (unaudited)	533,903	522,317	$ 0.16–0.53	$ 0.46

The number of options outstanding at September 30, 2004 includes 265,338 (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 441,235 shares with a weighted- average exercise price of $0.16 per share.

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

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
$0.16	1,784,809	9.21	922,243	$ 0.16
$0.26	6,072	9.92	126	0.26
	1,790,881		922,369	$ 0.16

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
$0.16	74,593	8.03	140,963	$ 0.16
$0.26	26,944	9.44	91,061	0.26
$0.53	420,780	9.61	11,479	0.53
	522,317		243,503	$ 0.21

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 386,778 (unaudited) options to employees to purchase shares of common stock at $0.53 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, 265,338 (unaudited) of these options had been exercised

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

at $0.53 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.

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	101	$ 0.16	$ 0.41	$ 0.25
March 31, 2003	15	0.16	1.35	1.19
June 30, 2003	642	0.16	3.62	3.46
September 30, 2003	12	0.16	5.14	4.98
December 31, 2003	6	0.26	6.55	6.29
March 31, 2004	1,402	0.26	7.99	7.73
June 30, 2004	499	0.53	10.79	10.26
September 30, 2004	2	0.53	13.59	13.06

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
			(unaudited)	
Research and development	$ —	$ 57	$ 39	$ 1,485
General and administrative	1	753	626	1,937
	$ 1	$810	$665	$ 3,422

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
			(unaudited)	
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%

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

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 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 2,428,805 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;
- 1,214,402 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.

Reverse Stock Split

On January 10, 2005, the Company's Board of Directors and stockholders approved a 1 for 1.6469 reverse stock split of the Company's common shares. Such stock split was effected on January 26, 2005. All common share and per share amounts contained in the financial statements were retroactively adjusted to reflect the stock split. As a result of the reverse stock split, the conversion ratio of the redeemable convertible preferred stock was adjusted such that each share of redeemable convertible preferred stock is convertible into approximately 0.6072 shares of common stock.

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	98	591
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	7,283	20,553
Weighted-average number of shares used in computing basic and diluted pro forma net loss per common share	7,381	21,144
Pro forma net loss per common share		
Basic and diluted	$ (6.66)	$ (0.74)

Table of Contents

Shares

Common Stock

PROSPECTUS

, 2005

Banc of America Securities LLC **CIBC World Markets**

Lazard **William Blair & Company**

Through and including , 2005 (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.

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	$ 12,327
NASD filing fee	9,120
NASDAQ National Market listing fee	100,000
Printing and engraving expenses	200,000
Legal fees and expenses	850,000
Accounting fees and expenses	600,000
Blue Sky qualification fees and expenses	5,000
Transfer agent and registrar fees and expenses	10,000
Miscellaneous fees and expenses	98,553
Total	$ 1,885,000

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.

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. All common share amounts below give effect to a 1 for 1.6469 reverse stock split of our common stock effected January 26, 2005. Following such stock split, each outstanding share of preferred stock is convertible into approximately 0.6072 shares of common stock and the exercise price of the warrant described below will be adjusted to $1.65 per share.

1. In October 2001, we sold 151,800 shares of common stock to George F. Tidmarsh, M.D., Ph.D., at $0.016469 per share, for an aggregate purchase price of $2,500.00.

2. In January 2002, we sold 22,770 shares of common stock to a former director at $0.16469 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 3,769,630 shares of our common stock with a weighted average price of $0.25 per share to a number of our employees, directors and consultants pursuant to our 2001 Equity Incentive Plan. As of September 30, 2004, 3,459,527 shares of common stock were issued upon exercise of certain of these options, of which 265,338 shares were subject to a call feature as of September 30, 2004, which call feature has since been cancelled.

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
3.5	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Registrant dated January 26, 2005
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	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, Mark G. Matteucci and Alan Colowick

EXHIBIT NUMBER	DESCRIPTION
10.16**	Change of Control Severance Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004
10.17**	Stock Vesting Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004
10.18	Letter Agreement amending Development Agreement by and between the Registrant and MediBIC Co. Ltd.
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. 6 to Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Redwood City, State of California, on the 28th day of January, 2005.

THRESHOLD PHARMACEUTICALS, INC.

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

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.

Signature	Title	Date
/s/ HAROLD E. SELICK Harold E. Selick	Director and Chief Executive Officer (principal executive officer)	January 28, 2005
* Janet I. Swearson	Chief Financial Officer (principal financial and accounting officer)	January 28, 2005
* George F. Tidmarsh	Founder, Director and President	January 28, 2005
* Michael F. Powell	Director	January 28, 2005
* Ralph E. Christoffersen	Director	January 28, 2005
* Patrick G. Enright	Director	January 28, 2005
* Wilfred E. Jaeger	Director	January 28, 2005
* William A. Halter	Director	January 28, 2005
* George G. C. Parker	Director	January 28, 2005
*/s/ HAROLD E. SELICK Attorney in fact		

Table of Contents

EXHIBIT INDEX

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
3.5	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Registrant dated January 26, 2005
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	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, Mark G. Matteucci and Alan Colowick
10.16**	Change of Control Severance Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004

Table of Contents

EXHIBIT NUMBER	DESCRIPTION
10.17**	Stock Vesting Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004
10.18	Letter Agreement amending Development Agreement by and between the Registrant and MediBIC Co. Ltd.
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.

Exhibit 3.5

CERTIFICATE OF AMENDMENT

OF THE

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

OF

THRESHOLD PHARMACEUTICALS, INC.

Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Corporation"), hereby certifies as follows:

1. The original Certificate of Incorporation was filed with the Secretary of State of Delaware on October 17, 2001.

2. A Certificate of Amendment of the Certificate of Incorporation was filed with the Secretary of State of Delaware on February 6, 2002.

3. An Amended and Restated Certificate of Incorporation was filed with the Secretary of State of Delaware on November 14, 2003.

4. Pursuant to Section 242 of the General Corporation Law of the State of Delaware, this Certificate of Amendment adds the following paragraph to the end of Article IV(A) of this Corporation's Amended and Restated Certificate of Incorporation:

"Upon the filing of this Certificate of Amendment with the Delaware Secretary of State (the "Effective Date"), each 1.6469 shares of the Common Stock of the Corporation issued and outstanding shall be reclassified and combined into one (1) share of Common Stock of the Corporation. There shall be no fractional shares issued. Stockholders who otherwise would be entitled to receive fractional shares shall be entitled to receive a cash payment in lieu thereof at a price equal to the fraction to which the stockholder would otherwise be entitled multiplied by the price per share of the Common Stock in the initial public offering of the Common Stock; provided, however, that in the event that the initial public offering of the Common Stock does not occur within ten (10) business days after the Effective Date, the Board of Directors shall determine the fair market value of one share of Common Stock as of the Effective Date for purposes of such cash payment. The ownership of a fractional interest will not give the holder thereof any voting, dividend or other rights except to receive payment therefore as described herein."

5. The foregoing Certificate of Amendment has been duly adopted by this corporation's Board of Directors and stockholders in accordance with the provisions of the Corporation's Amended and Restated Certificate of Incorporation and with Sections 242, 245 and 228 of the General Corporation Law of the State of Delaware.

This Certificate of Amendment is executed at Redwood City, California, January 26, 2005.

THRESHOLD PHARMACEUTICALS, INC.

By: /s/ HAROLD E. SELICK

Dr. Harold E. Selick,
Chief Executive Officer

Exhibit 4.1

COMMON STOCK

NUMBER

THRESHOLD
PHARMACEUTICALS

COMMON STOCK

SHARES

INCORPORATED UNDER THE
LAWS OF THE STATE OF DELAWARE

SEE REVERSE FOR
CERTAIN DEFINITIONS

CUSIP 885807 10 7

This Certifies that

is the record holder of

FULLY PAID AND NONASSESSABLE SHARES OF COMMON STOCK, $.001 PAR VALUE, OF

THRESHOLD PHARMACEUTICALS, INC.

transferable on the books of the Corporation by the holder hereof in person or by duly authorized attorney upon the surrender of this certificate properly endorsed. This certificate is not valid until countersigned by the Transfer Agent and registered by the Registrar.

WITNESS the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

CERTIFICATE OF STOCK

Dated:

CHIEF FINANCIAL OFFICER,
VICE PRESIDENT FINANCE AND OPERATIONS

SEAL

CHIEF EXECUTIVE OFFICER

COUNTERSIGNED AND REGISTERED:
MELLON INVESTOR SERVICES LLC
TRANSFER AGENT AND REGISTRAR

AUTHORIZED SIGNATURE

COMMON STOCK **COMMON STOCK**

THLD

INCORPORATED UNDER THE
LAWS OF THE STATE OF DELAWARE

SEE REVERSE FOR
CERTAIN DEFINITIONS

CUSIP 885807 10 7

This Certifies that

is the record holder of

FULLY PAID AND NONASSESSABLE SHARES OF COMMON STOCK, $.001 PAR VALUE, OF

THRESHOLD PHARMACEUTICALS, INC.

transferable on the books of the Corporation by the holder hereof in person or by duly authorized attorney upon the surrender of this certificate properly endorsed. This certificate is not valid until countersigned by the Transfer Agent and registered by the Registrar.

WITNESS the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

Dated:

[SEAL]

CHIEF FINANCIAL OFFICER,
VICE PRESIDENT FINANCE AND OPERATIONS

CHIEF EXECUTIVE OFFICER

COUNTERSIGNED AND REGISTERED:
MELLON INVESTOR SERVICES LLC
TRANSFER AGENT AND RETISTRAR

AUTHORIZED SIGNATURE

THRESHOLD PHARMACEUTICALS, INC.

The Corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional, or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Such requests shall be made to the Corporations's Secretary at the principal office of the Corporation.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM-	as tenants in common
TEN ENT-	as tenants by the entireties
JT TEN-	as joint tenants with right of survivorship and not as tenants in common

UNIF GIFT MIN ACT- _____ (Cust) Custodian _____ (Minor)
under Uniform Gifts to Minors Act _____ (State)

UNIF TRF MIN ACT- _____ (Cust) Custodian (until age_____)
_____ (Minor) under Uniform Transfers to Minors Act _____ (State)

Additional abbreviations may also be used though not in the above list.

FOR VALUE RECEIVED, _____ hereby sell, assign and transfer(s) unto _____

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

_____

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING ZIP CODE OF ASSIGNEE)

_____

_____

_____ Shares

of the Common Stock represented by the within Certificate, and do(es) hereby irrevocably constitute and appoint

_____ Attorney

to transfer the said stock on the books of the within named Corporation with full power of substitution in the premises.

Dated_____ X _____

X _____

NOTICE: THE SIGNATURE TO THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME(S) AS WRITTEN UPON THE FACE OF THE CERTIFICATE IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATEVER.

SIGNATURE(S) GUARANTEED:

By _____

THE SIGNATURE(S) MUST BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION. (BANKS, STOCKBROKERS, SAVINGS AND LOAN ASSOCIATIONS AND CREDIT UNIONS WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM), PURSUANT TO S.E.C. RULE 17Ad-15.

KEEP THIS CERTIFICATE IN A SAFE PLACE. IF IT IS LOST, STOLEN, OR DESTROYED THE CORPORATION WILL REQUIRE A BOND OF INDEMNITY AS A CONDITION TO THE ISSUANCE OF A REPLACEMENT CERTIFICATE.

EXHIBIT 5.1

HellerEhrman
ATTORNEYS

January 28, 2005

Threshold Pharmaceuticals, Inc.
1300 Seaport Blvd.
Redwood City, CA 94063

Registration Statement on Form S-1

Ladies and Gentlemen:

We have acted as counsel to Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Company"), in connection with the Registration Statement on Form S-1 (Registration No. 333-114376) filed with the Securities and Exchange Commission on April 9, 2004 (as may be further amended or supplemented, the "Registration Statement") for the purpose of registering under the Securities Act of 1933, as amended, 6,133,333 shares of its authorized but unissued Common Stock, par value $.001 per share (the "Shares"). The Shares, which include up to 800,000 shares of the Company's Common Stock issuable pursuant to an over-allotment option granted to the underwriters, are to be sold pursuant to an Underwriting Agreement (the "Underwriting Agreement") among the Company and Banc of America Securities LLC and CIBC World Markets Corp., as representatives of the several underwriters named in Schedule A to the Underwriting Agreement.

We have assumed the authenticity of all records, documents and instruments submitted to us as originals, the genuineness of all signatures, the legal capacity of natural persons and the conformity to the originals of all records, documents and instruments submitted to us as copies.

In rendering our opinion, we have examined the following records, documents and instruments:

(a) The Amended and Restated Certificate of Incorporation of the Company, filed as an exhibit to the Registration Statement and to be filed with the Delaware Secretary of State in connection with the sale of the Shares, and certified to us by an officer of the Company as being the form to be filed with the Delaware Secretary of State in connection with the sale of the Shares;

(b) The Bylaws of the Company certified to us by an officer of the Company as being complete and in full force and effect as of the date of this opinion;

(c) A Certificate of an officer of the Company (i) attaching records certified to us as constituting all records of proceedings and actions of the Board of Directors,

including any committee thereof, and stockholders of the Company relating to the Shares, and the Registration Statement, and (ii) certifying as to certain factual matters;

(d) The Registration Statement; and

(e) A draft of the Underwriting Agreement to be filed as Exhibit 1.1 to the Registration Statement.

This opinion is limited to the federal law of the United States of America and the General Corporation Law of the State of Delaware, and we disclaim any opinion as to the laws of any other jurisdiction. We further disclaim any opinion as to any other statute, rule, regulation, ordinance, order or other promulgation of any other jurisdiction or any regional or local governmental body or as to any related judicial or administrative opinion.

Based upon the foregoing and our examination of such questions of law as we have deemed necessary or appropriate for the purpose of this opinion, and assuming that (i) the Registration Statement becomes and remains effective during the period when the Shares are offered and sold, (ii) the Underwriting Agreement signed by the parties thereto conforms in all material respects to the draft to be filed as Exhibit 1.1 to the Registration Statement, (iii) the Shares are issued, delivered and paid for in accordance with the terms of the Underwriting Agreement, (iv) appropriate certificates evidencing the Shares will be executed and delivered by the Company, and (v) all applicable securities laws are complied with, it is our opinion that, when issued by the Company, the Shares will be legally issued, fully paid and nonassessable.

This opinion is rendered to you in connection with the Registration Statement and we disclaim any obligation to advise you of any change of law that occurs, or any facts of which we may become aware, after the date of this opinion.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement and to the reference to us under the caption “Legal Matters” in the Registration Statement.

Very truly yours,

/s/ Heller Ehrman White & McAuliffe LLP

EXHIBIT 10.10

***CERTAIN INFORMATION IN THIS EXHIBIT HAS BEEN OMITTED AND FILED SEPARATELY WITH THE COMMISSION. CONFIDENTIAL TREATMENT HAS BEEN REQUESTED WITH RESPECT TO THE OMITTED PORTIONS.**

Agreement

between

Aziende Chimiche Riunite Angelini Francesco – Acraf S.p.a., having its registered office in Viale Amelia, 70—00181 Rome Italy c.f.01312320680, p.Iva 049290810000 a company incorporated under the laws of Italy (hereinafter referred to as **"Acraf"**)

and

Threshold Pharmaceuticals, Inc., having its registered office at 951 Gateway Blvd., Ste. 3A, South San Francisco, CA 94080, USA, a company incorporated under the laws of the State of Delaware of the United States (hereinafter referred to as **"TH"**)

Effective on the date of the last signature of this Agreement (hereinafter referred to as **"Effective Date"**).

Whereas

— Acraf and TH are companies involved in the research, development and commercialization of pharmaceutical products;
— Acraf owns the rights to the dossier for a tableted product containing 30 tablets per package, as previously approved in Italy, Austria, and Portugal for use as a single agent in the treatment of brain, breast, prostate, and lung cancer (hereinafter referred to as the **"Product"**), each tablet containing 150 mg of the active ingredient Lonidamina (hereinafter referred to as the **"Active Ingredient"**), such dossier including but not limited to all documents that have been or may in the future be filed or submitted to any regulatory authority anywhere in the world and communications to or from such Authorities in connection with the Active Ingredient or Product, and information pertaining to the pre-clinical and clinical development of the Active Ingredient and Product, manufacturing processes for the Active Ingredient and finished Product, specifications, and analytical and validation methods used by Acraf to manufacture the Active Ingredient and the Product (such documents and information collectively hereinafter referred to as the **"Dossier"**);
— Acraf declares it has the sole and exclusive right to dispose of all the rights regarding the Dossier;
— TH is willing to be granted by Acraf the right to use the Dossier as provided in Art.1.1 below for the purpose of facilitating TH's efforts to develop and market products equivalent to the Product as well as new unit dosage forms and other products containing the Active Ingredient ("TH Products");
— TH is willing to purchase a certain amount of Active Ingredient manufactured by Acraf to carry out one or more of the clinical studies required for the approval of TH Products, which clinical studies include but are not limited to those studies contemplated by the development plan (hereinafter referred to as **"Development Plan"** or **"DP"**) as described in the Annex **A** to this Agreement and those studies mentioned in the following

Now, therefore, in consideration of the premises and
of the mutual covenants herein contained and of other good and valuable
consideration, the parties hereto agree as follows:

1. Subject

1.1 Acraf does hereby grant to TH, and TH does hereby accept:

i) the co-exclusive rights of utilising the Dossier and its contents for obtaining marketing authorisations in the territory described in Annex **C** (hereinafter referred to as **"Acraf Territory"**) for a TH Product equivalent to the Product previously marketed by Acraf in Italy and of conducting any additional studies TH determines in its sole discretion to undertake for modifying the Dossier if such studies are requested by the Italian Health Authority or another health authority where the Dossier is now filed, such additional studies to be conducted only as TH deems appropriate and at its own costs and granting to Acraf the right to use any such additional studies free of any charge solely in connection with obtaining additional regulatory approvals for use of the Product in Italy to treat the existing approved, and any new, cancer indications (hereinafter referred to as **"THL1"**); for THL1, semi-exclusive rights means that in addition to TH, Acraf will have the right – with no limitation – to use and/or to grant to any third parties the same rights granted by Acraf to TH for THL1; THL1 also includes Acraf's agreement to provide TH such licenses or other documentation to enable TH to market as soon as possible after the expiry of the remaining stocks of Product on the market (which expiry occurs in [***]) a TH Product equivalent to the Product or the Product itself;

ii) the exclusive rights of utilising the Dossier and its contents for obtaining marketing authorisations of a TH Product equivalent to the Product in the territory described in Annex **B** (hereinafter referred to as **"TH Territory"**) and of conducting any additional studies TH determines in its sole discretion to undertake for modifying or otherwise using the Dossier if requested by the relevant health authority, such additional studies to be conducted at its own costs and granting to Acraf the right to use the results of such additional studies free of any charge only as necessary for compliance with the regulatory requirements to maintain the marketing authorization to use the Product in Italy to treat cancer indications (hereinafter referred to as **"THL2"**); for THL2, exclusive rights means that in addition to TH no other company will have granted by Acraf any of the rights granted to TH in respect of THL2;

iii) the exclusive right of utilising the Dossier and its contents for carrying out clinical studies related to the anti-cancer activity of the Active Ingredient as set forth in the **DP** (hereinafter referred to as **"THL3"**);
for THL3, exclusive rights means that in addition to TH no other company will have granted by Acraf any of the rights granted to TH

in respect of THL3; and

iv) the exclusive right of utilising the Dossier and its contents in the TH Territory and the Acraf Territory for

1) writing a new registration dossier of one or more TH Products (hereinafter referred to as **"New Dossier"**);

2) filing the New Dossier to obtain the relevant marketing authorisations in the TH Territory and the Acraf Territory (hereinafter referred to as **"THL4"**);

for THL4, exclusive rights means that in addition to TH no other company will have granted by Acraf any of the rights granted to TH in respect of THL4, such THL4 being subject to Acraf's semi-exclusive rights set forth in Art.1.2.A, below;

(THL1, 2, 3, and 4 hereinafter jointly referred to as **"TH Licence"**).

1.2 In consideration of the THL3 and 4 granted by Acraf to TH, TH does hereby:

A grant to Acraf, and Acraf does hereby accept:

i) the exclusive right, subject only to those held by TH and its sublicensees, which have co-extensive rights, to use the Results, as defined in the following Art.5.2, at the end of the DP in the Acraf Territory for

1) writing a dossier relating to the use of the Product or an equivalent TH Product for a cancer indication other than the indications for which the Product was approved prior to the Effective Date;

2) filing the resulting dossier to obtain any relevant marketing authorisations in the Acraf Territory;

ii) in the event that the Results as defined in the following Art.5.2, shall be patentable, the exclusive right – free of any charge—to use the relevant Patent, as described in the following Art.5.1.—in the Acraf Territory for the same purposes described in the previous Art.1.2.A.i) (hereinafter referred to as **"Acraf Licence"**);

Parties agree that:

— for the licence described in the previous Art.1.2.A.i), exclusive rights means that in addition to Acraf, only TH and its sublicensees will have the right to use the Results in Acraf Territory according to the rights granted to TH by Acraf with respect to THL4;

— for the licence described in the previous Art.1.2.A.ii), exclusive rights means that in addition to Acraf, in Acraf Territory no company other than TH and its sublicensees will have the same rights granted pursuant to the licence described in the previous Art.1.2.A.ii);

B undertakes to offer to Acraf—for a period starting on the second anniversary of the Effective Date and lasting until 10 (ten) years after the date of the first launch of the first TH Product—the right to provide 75% (seventy-five percent) of all the Active Ingredient needed by TH at a price equal to or lower than the price which TH would otherwise be required to pay to a third party Active Ingredient manufacturer, as notified in writing by TH to Acraf; provided, however, that if Acraf does not agree to the same price, timelines, terms and conditions offered by the third party manufacturer within [***] ([***]) days of receipt of the price,

timelines, terms and conditions from TH, then this right shall lapse and TH shall be free, in its sole discretion, to purchase its Active Ingredient requirements from such third party manufacturer or any other manufacturer without further notice to Acraf (hereinafter referred to as **"Supply Right"**) (Acraf Licence and Supply Right hereinafter jointly referred to as **"Acraf Rights"**).

1.3 Parties agree that each shall have the right to sublicense their respective rights described in the previous Art.1.1 and 1.2 to third parties except as otherwise prohibited in this Agreement.

1.4 Parties agree that the name of each sublicensee will have to be disclosed to the other Party and Parties declare and warrant that each sublicensee will satisfy any obligations applicable to such sublicensee described in this Agreement.

1.5 Parties agree that the THL3 and 4 are considered as fair consideration for Acraf Rights, and Acraf Rights are considered as fair consideration for THL3 and 4, and that no other payments shall be made by Acraf to TH or by TH to Acraf to use without limitation the rights granted each other pursuant to the above mentioned licences.

1.6 For having granted the THL 1 and 2, TH shall pay the following amount to Acraf upon the occurrence of the events specified below:

a) a one-time payment of €300.000,00 (three-hundred thousand Euro) to be paid within [***] days of the Effective Date;

b) a [***] payment of €[***] ([***] Euro) to be paid within [***] ([***]) days from the date of publishing of the Marketing Authorisation for the first TH Product authorized for sale in the Acraf Territory;

c) a [***] payment of €[***] ([***] Euro) to be paid within [***] ([***]) days from the date of publishing of the Marketing Authorisation for the first TH Product authorized for sale in the TH Territory;

d) a [***] payment of €[***] ([***] Euro) if and when the TH Net Sales **("TH Net Sales"** means the sales of TH Products made by TH – directly or through its sublicensees—at the prices invoiced to the customers less taxes relating to such sales, returns, cash and quantity discount granted to customers, such cash and quantity discounts limited to [***]% ([***] per cent) made in the TH Territory) exceeds €50.000.000,00 (fifty million Euro)), to be paid within [***] ([***]) days after the date of notification of the relevant sales report as described in Art.1.7.b).

e) other than the payments required by Art.1.6.a, and the payments that may be required if the conditions of Art1.6.b-d are met, and the payment due upon Acraf's fulfilment of its obligation under Art.3, this Agreement does not impose any additional payment obligations on TH; thus, TH shall have no obligation under this Agreement to pay any amount in excess of [***] ([***] Euros) to Acraf during the term of this Agreement or thereafter.

1.7 TH undertakes to report to Acraf:

a) the date on which all the marketing authorisation applications have been made and the date on which all the relevant Marketing Authorisations have been obtained in Acraf Territory and in TH Territory according to what is provided in the previous Art.1.1. within 30 (thirty) days from the application date and from the date on which the above mentioned Marketing Authorisation have been

obtained;

b) within 30 (thirty) days from the end of each year period starting from January 1, 2005, the report of TH Net Sales for the calendar year then ended, such reporting obligation to terminate upon the payment, if any, of the one-time payment described in Art.1.6.d.

2. Development Plan

2.1 TH undertakes to use reasonable business efforts to complete the DP within sixty (60) months from the Effective Date of this Agreement (hereinafter referred to as **"DPTerm"**).

2.2 TH shall be free to use the Dossier in connection with the TH Licence after TH makes the payment described in the Art.1.6.a).

2.3 After TH makes the payment described in the Art. 1.6.a), Acraf shall deliver to TH a copy of the Dossier in its possession.

2.4 TH shall keep Acraf informed on a regular and continual basis concerning the activities conducted by it pursuant to the DP.

2.5 Within twelve (12) months from the end of the DP, TH undertakes to notify Acraf in writing – with a registered letter – of the Results (hereinafter referred to as **"Notification"**).

2.6 Any and all fees in conjunction with the assignment of the right to use the Dossier and with the carrying out of the DP shall be borne by TH.

2.7 The DP may be modified by TH only by written notification to Acraf and after written approval, which shall not be unreasonably withheld, by Acraf.

3. Active Ingredient

3.1 Acraf undertakes to sell to TH an amount of Kg 22 (twenty-two] of Active Ingredient manufactured on [***] – with an expiry date on [***]—suitable for use in TH Products as better described in the analytical document to be delivered as provided in the following Art.3.2 (hereinafter referred to as **"Amount"**).

3.2 The Amount shall be supplied by Acraf in bulk with all the relevant analytical documents updated to the Effective Date.

3.3 The delivery time from Acraf to TH shall not exceed 60 (sixty) days starting from the Effective Date of this Agreement.

3.4 Acraf undertakes to deliver the Amount ex works Acraf's plant of Via Guardapasso 1, 04011 Aprilia (Latina).

3.5 The price of the Amount will be €75.000,00 (seventy five thousand/00) euros (hereinafter referred to as **"Payment"**) to be paid within 30 (thirty) days from the invoice date.

4. Duration

4.1 Parties agree that:

a) the Acraf Licence shall commence on the Effective Date of this Agreement and shall extend for a term of 15 (fifteen) years after the date of first launch – directly by Acraf or through any third party appointed as sublicensee by Acraf—of any Product that expires after November, 2004, in the Acraf Territory;

b) the Supply Right shall commence on the second anniversary of the Effective Date and shall extend for a term of 10 (ten) years after the date of first launch – made directly by TH or through any third party appointed as sublicensee by TH—of the first TH Product in the TH Territory and as provided in Art. 1.2B and

c) the TH Licence shall commence on the Effective Date and shall extend for a term of 15 (fifteen) years after the date of first launch – directly by TH or through any third party appointed as sublicensee by TH—of the first TH Product in the TH Territory.

4.2 Parties agree that at the end of the Acraf Licence and of the TH Licence, Acraf will remain owner and holder of all the marketing authorisations for the Product obtained by Acraf in the Acraf Territory and TH will remain owner and holder of all the marketing authorisations for TH Products obtained by TH in the TH Territory and in the Acraf Territory. Any termination or expiration of this Agreement shall not act to divest a Party of any interest in any regulatory filing or authorization made prior to the effective date of such termination or expiration.

5. Results and Intellectual Property Rights

5.1 It is expressly agreed between the Parties that TH shall not acquire any intellectual property rights with respect to the Dossier other than the right described in the previous Art.1.1 and elsewhere in this Agreement, and that TH shall have the ownership of the Results as defined in the following Art.5.2 and any patents relating to such Results (hereinafter referred to as **"Patent"**).

5.2 Parties agree to define as **"Results"** all technical information, formulations, processes, know-how, data, specifications, characterization methods and results, and other proprietary information, whether or not patented or patentable, only and exclusively related to the anti-cancer activity of the Active Ingredient obtained by TH in the clinical trials carried out pursuant to the DP.

6. Confidentiality

6.1 Parties agree to define as **"Confidential Information"** all information exchanged by the parties relating to the Dossier, any modification thereof, any New Dossier, DP, or otherwise provided to a Party under this Agreement. Parties agree that documents and information contained in the Dossier will be used by TH in seeking regulatory approval of TH Products and by Acraf in seeking additional regulatory approvals of Product and so may enter the public domain as such additional indication is, or such TH Products are, approved.

6.2 Each of the Parties shall hold in confidence any and all Confidential Information disclosed to it by the other party before and during the term of this Agreement and shall not use such Confidential Information except in accordance with the terms of this Agreement.

6.3 Neither party shall, without the prior written consent of the other party, disclose to any third party (except to regulatory authorities to obtain and maintain patents, product registrations or other disclosures required by

law) or use for its own purposes any Confidential Information of the other party except in connection with the development and registration of the Product and TH Products.

6.4 The provisions of this Art.6 shall survive the expiry or termination of the Agreement until all of the Confidential Information has fallen within one of the exceptions set forth in this Art.6.

6.5 The obligation of confidentiality under this Art.6 shall not apply to any data or information disclosed by one party to the other which:

6.5.1 at the time of the disclosure or thereafter is in or comes into the public domain by publication or otherwise, through no fault of either party;

6.5.2 is disclosed to the recipient by a third party having legal right to make such disclosure;

6.5.3 is previously known to the recipient at the date of disclosure; or

6.5.4 is required by law to be disclosed, provided that, except in connection with seeking regulatory approval for the Product and TH Products, the disclosing party furnishes the other party with written notice that the data or information is proposed to be disclosed sufficiently in advance of the proposed disclosure so as to provide the other party with reasonable opportunity to seek to prevent the disclosure of or to obtain a protective order for the data or information.

6.6 Further, each party shall be entitled to disclose any Confidential Information received by its responsible employees and officers, including any such employees and officers of any of their Affiliates, on a "need-to-know-basis" for the proper performance of this Agreement and for the negotiation and performance of any licenses and sublicenses hereunder.

6.7 The parties shall impose at least the same degree of confidentiality on each such employee and officer or other recipient as is imposed upon the parties under this Agreement with respect to confidential information, and shall be responsible to the disclosing party for any breaches of confidentiality made by such persons.

7. Amendment

This Agreement may be amended only by a written instrument signed by both Parties.

8. Good Faith

8.1 Any provision of this Agreement that is held to be inoperative, unenforceable or invalid in any jurisdiction shall be inoperative, unenforceable or invalid in that jurisdiction without affecting any other provision hereof in that jurisdiction or the operation, enforceability or validity of that provision in any other jurisdiction, and to this end the provisions hereof are declared to be severable.

8.2 Subject to this, such provision will be renegotiated by the parties in such a way as to render the same lawful and to achieve, to the extent possible, the economic, business and other intent of the original provisions.

8.3 Each party has considered this Agreement and it is the good faith belief of each party that the Agreement is in accordance with the national and

supranational treaties, laws, rules and regulations applicable hereto.

9. Force Majeure

9.1 In this Agreement, **"Force Majeure"** means an event or occurrence beyond the reasonable control of a party which by the exercise of reasonable diligence could not be overcome, including, but not limited to, strikes, lock-outs, labour disruptions, acts of God, changes in the law, restraints of governments, riots, arrests of people, act of war, civil disturbances, rebellion or sabotage, fire, flood, lightning, earthquake, epidemic, not caused by the act or omission of the party, any delay or failure by a governmental authority to issue any relevant permit or order not caused by the act or omission of the party.

9.2 A party shall be deemed not to be in default with respect to non-performance of any of its obligations under this Agreement, if and so long as such non-performance is due in whole or in some material way to an event of Force Majeure and that party has used its commercially reasonable efforts to remove the event of Force Majeure and to perform its obligations under the Agreement. If an event of Force Majeure occurs, the party affected shall promptly notify the other party of the occurrence of the event, its extent and probable duration and will use its best endeavors to overcome the difficulties created thereby and to resume performance of its obligations as soon as practicable.

9.3 If a party's failure to perform any of its obligations due to a Force Majeure has continued for thirty (30) days, unless within such period the non-performing party has begun to substantially remedy its inability to perform, and will be in a position to fully resume its performance obligations within a further thirty (30) days thereafter, the other party may, if itself not in default under the Agreement, terminate this Agreement by providing written notice to the non-performing party. In the event of such termination, both parties' respective rights and obligations under this Agreement shall terminate except for vested rights and any amounts previously due and owing by one party to the other and except for any other obligations which this Agreement expressly provides shall survive termination, or which should, by their nature, so survive.

10. Communication

Any notice or request with reference to this Agreement shall be made by registered mail; return receipt requested and shall be directed by one party to the other at its respective following address:

—Acraf: Attn.to Maria Rita Luparini
P.le della Stazione snc, 00040 S.Palomba, Pomezia,
Rome, Italy

—TH: Attn. to Dr. George Tidmarsh, President
Threshold Pharmaceuticals, Inc.
951 Gateway Blvd., Suite 3A
South San Francisco, CA 94080 USA

11. Applicable Law and Jurisdiction

11.1 This Agreement shall be governed and construed in accordance with the laws of Delaware, U.S.A

11.2 In case the dispute cannot be settled amicably, the place of performance and venue for all disputes arising out of this contract will be London, England.

12. Relationship of the Parties

12.1 The relationship between the parties created pursuant to this Agreement is intended to and shall be solely that of independent contractors.

12.2 Neither party, nor its employees, agents or representatives shall under any circumstances be considered employees, agents, partners, joint venturers or representatives of the other party.

12.3 Neither party, nor their employees, agents or representatives shall act or attempt to act, or represent itself, directly or by implication, as an employee, agent, joint venturer, partner or representative of the other party or in any manner assume or create, or attempt to assume or create, any obligation or liability of any kind, express or implied, on behalf of or in the name of the other party.

13. Further Assurances

Each party will at any time and from time to time, upon the request of the other party, execute and deliver such further documents and do such further acts and things as the other party may reasonably request to evidence, carry out and give full effect to the terms, conditions, intent and meaning of this Agreement.

14. Entire Agreement, Waiver, Amendment.

14.1 This Agreement, together with Annexes A, B and C hereto, supersedes any prior agreements between the parties as to the subject matter of the Agreement, whether oral or in writing, and contains the entire understanding between the parties as to the subject matter of the Agreement.

14.2 Any Confidential Information previously disclosed by the parties in respect of such subject matter shall now be subject to the confidentiality provisions hereof.

14.3 No delay or failure on the part of a party in exercising any rights under this Agreement shall affect any of such party's other rights.

14.4 This Agreement may not be modified or amended except by further instrument duly executed by the authorized representatives of both parties.

14.5 The preamble to this Agreement shall form an integral part of this Agreement and be binding on the parties hereto.

15. Other provisions

15.1 Amendments and supplements to this Agreement must be made in writing in order to take effect.

15.2 Should a provision of this Agreement be or become legally ineffective or should a gap in the Agreement be ascertained, this shall not have an effect on the validity of the remaining provisions.

15.3 A reasonable provision shall become valid which comes closest to the commercial aim of this Agreement and the intention of the parties as far as legally possible instead of the ineffective provision or in order to fill in the gap.

Aziende Chimiche Riunite Angelini Francesco Acraf S.p.a.	Threshold Pharmaceuticals, Inc.
/s/ Walter Frosecchi	/s/ George Tidmarsh
Date, 6/24/2004	Date, 6/24/2004

Annex **A**
Development Plan

[***] trial
TH provided clinical trial funding to a recently completed trial of Product in combination with other anti-cancer agents at a site in Italy. Over the next six months, this data will be analyzed to determine if the results warrant further clinical development for this indication. The Results will be shared under confidentiality with Acraf.

If an [***] trial is not pursued, TH contemplates undertaking either a trial in [***], a trial in [***] and [***] or [***], as described below.

[***] trial
TH is evaluating whether to initiate clinical development of the Product or a TH Product in certain [***] indications, including for [***] in [***] or [***]. The trial would be a [***] trial of no more than [***] patients [***], start in [***], and have a [***] duration.
TH could use the Product or an equivalent TH Product in such a trial.

[***] trial
TH is evaluating whether to initiate clinical development in [***] and [***] in [***], including for [***] and [***] in [***] with [***] or for [***] in [***]. The trial would be similar in timelines, size, and duration as described above. TH could use the Product or an equivalent TH Product in such a trial.

Annex **B**
TH Territory

TH Territory means all the countries of the world that are not in the Acraf Territory

Annex **C**
Acraf Territory

EU Members
Austria,
Belgium,
Cyprus,
Czech Republic,
Denmark,
Estonia,
Finland,
France,
Germany,
Greece,
Hungary,
Ireland,
Italy,
Latvia,
Lithuania,
Luxembourg,
Malta,
Netherlands,
Poland,
Portugal
Slovakia,
Slovenia,
Spain,
Sweden,
United Kingdom

EEA Members
Iceland,
Liechtenstein,
Norway

Others
Bosnia-Herzegovina
Bulgaria
Croatia
Rep. of Macedonia
Romania
San Marino
Vatican
Yugoslavia
Armenia
Azerbajan
Belorussia
Georgia
Kazakhstan
Kirghizistan
Rep. of Moldova
Tadjikistan
Ukraina
Uzbekistan

EXHIBIT 10.14

DEVELOPMENT

AGREEMENT

BETWEEN

THRESHOLD PHARMACEUTICALS, INC.

AND

MEDIBIC CO., LTD.

DEVELOPMENT AGREEMENT

THIS AGREEMENT is entered into as of the 30th day of November, 2004, ("Effective Date") by and between**THRESHOLD PHARMACEUTICALS, INC.,** a Delaware corporation having its principal place of business at 951 Gateway Blvd., Suite 3A, South San Francisco, CA 94080, U.S.A. ("Threshold"), and **MEDIBIC CO., LTD.,** a Japan corporation, having its head office at Daido Seimei Kasumigaseki Building 8F, 1-4-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan ("MediBIC").

RECITALS

WHEREAS, Threshold is engaged in the research and development of therapeutic pharmaceutical products and desires funding and development expertise to support the development in Asia of its glufosfamide product candidate;

WHEREAS, MediBIC is also engaged in the development of therapeutic pharmaceutical products; and

WHEREAS, Threshold and MediBIC desire to establish a relationship to develop in Asia a therapeutic product containing glufosfamide for the treatment of cancer;

NOW, THEREFORE, in consideration of the foregoing and the covenants and promises contained herein, the parties agree as follows:

ARTICLE 1

DEFINITIONS

As used herein, the following terms shall have the following meaning, and the singular shall include the plural and vice versa:

1.1 "Affiliate" shall mean any corporation or other entity which controls, is controlled by, or is under common control with a party. A corporation or other entity shall be regarded as in control of another corporation or entity if it owns or directly or indirectly controls more than fifty percent (50%) of the voting stock or other ownership interest of the other corporation or entity, or if it possesses, directly or indirectly, the power to direct or cause the direction of the management and policies of the corporation or other entity or the power to elect or appoint more than fifty percent (50%) of the members of the governing body of the corporation or other entity. Notwithstanding the foregoing, in no event shall any corporation or other entity in which MediBIC holds a equity or other ownership interest greater than 5% be deemed a Threshold Affiliate.

1.2 "Agreement" shall mean this Development Agreement.

1.3 "Asian Territory" shall mean Japan, North Korea, South Korea, China, Taiwan, Hong Kong, Indonesia, the Philippines, Thailand, Vietnam, Malaysia, Myanmar, Singapore, Cambodia, Laos, Bangladesh, India, and Brunei.

1.4 "Commercialization" shall mean all activities that are undertaken during the term of this Agreement that relate to the commercial manufacture, marketing, and sale of Compound Product in the Asian Territory, including advertising, education, planning, marketing, promotion, distribution, market and product support studies for the Compound Product in the Asian Territory.

1.5 "Compound" shall mean glufosfamide.

1.6 "Compound Product" shall mean any product that was developed by Threshold or a sublicensee of Threshold for marketing as a therapeutic that contains the Compound and that is for the treatment of cancer.

1.7 "Confidential Information" shall mean, subject to the limitations set forth in Section 8.1 hereof, information disclosed to one party by the other party.

1.8 "Development Plan" shall mean the plan agreed upon by the Parties under Article 4 of this Agreement for the development of Compound Product.

1.9 "Field" shall mean all human cancer therapeutic uses.

1.10 "First Indication" means that particular type of cancer that the Development Plan, agreed upon by the Parties, describes as the first cancer indication for which regulatory approval for the Compound Product will be sought in the Asian Territory.

1.11 "Initiation" means, with respect to the particular phase of a clinical trial (e.g., Phase I, Phase II or Phase III), the dosing of the first human patient in such trial.

1.12 "Japanese Pharmaceutical Company" shall mean a pharmaceutical company that maintains its corporate headquarters and its principal place of business in Japan.

1.13 "MediBIC Know-How" shall mean, to the extent MediBIC is free to grant rights therein and it is necessary and useful for the development, manufacture or sale of Compound Product, all tangible or intangible know-how, trade secrets, inventions (whether or not patentable), data, clinical and preclinical results, information, and any physical, chemical or biological material, including cell lines, any replication or any part of such material, which MediBIC owns, controls or has a license to (with right to sublicense) during the term of this Agreement.

1.14 "MediBIC Payment" shall mean the payment made by MediBIC to Threshold per the terms of Article 3.

1.15 "MHW" shall mean the Japanese Ministry of Health and Welfare or such other agency or instrumentality of Japan to which the responsibilities and authority of the MHW are given or delegated from time to time.

1.16 "Net Revenues" shall mean, for purposes of Section 6.1, the upfront fees, milestone payments and royalties received by Threshold in the Asian Territory for the development and Commercialization of the Compound Product, excluding the US$4,750,000 to be paid by MediBIC as described in Section 3.1 of this Agreement, less any royalties and other milestones owed by

Threshold to a third party for such development and Commercialization. The Parties agree that, with respect to the up-front and any milestone payments that have been or are later paid to Baxter International, Inc., or its affiliates ("Baxter") by Threshold pursuant to Threshold's license agreement with Baxter for licensing of the Compound, one-third of such payments shall be attributable to development and Commercialization of Compound Product in the Asian Territory and therefore deducted from gross revenue. All of the subsequent royalties owed to Baxter for sales of Compound Product in the Asian Territory shall be deductible from gross revenues. For purposes of this definition, "gross revenue" shall mean, in the event that Threshold sublicenses a third party to develop and/or Commercialize Compound Product in the Asian Territory, the milestones and royalty payments received by Threshold from said third party.

1.17 "Net Sales" shall mean, for purposes of Section 6.2, with respect to a Compound Product, the gross amounts received for all quantities of such Compound Product sold by Threshold and its Affiliates to independent third parties in the Asian Territory after deducting (a) trade, quantity and cash discounts actually taken, (b) returns, rebates and allowances (including in connection with any Compound Product withdrawals or recalls), (c) duties, sales and excise taxes or other governmental charges, (d) transportation, delivery and insurance charges, (e) commissions or fees paid to third parties in connection with such sales to the extent not deducted above; (f) retroactive price reductions imposed by public authorities, and (g) sales for use in clinical trials or other scientific testing. With respect to sales of combination products, which shall consist of Compound Products combined with one or more other active ingredients, products or services, "Net Sales" from such sales shall be calculated by multiplying the Net Sales of that combination by the fraction A/(A + B), where A is the average gross selling price of the Compound Product sold separately in that country, and B is the average gross selling price of the other product, active ingredient or service sold separately in that country. In the event that no separate sale of such other product, active ingredient or service is made during the applicable royalty reporting period and in the relevant country in which the sale of the combination product was made, then Net Sales shall be determined by multiplying the Net Sales of such combination by a fraction (C/(C+D)), where C is Threshold's or its Affiliate's standard fully-burdened cost of the Compound Product and D is Threshold's or its Affiliate's standard fully-burdened cost of the relevant other product, active ingredient or service. Sales among Threshold and its Affiliates shall not be deemed Net Sales; provided, however, that any sales by Threshold or its Affiliates to independent third parties shall be deemed Net Sales. In the event a Threshold sublicensee sells Compound Product in the Asian Territory, then, for purposes of determining whether payments are owed MediBIC under Section 6.3 of this Agreement, Net Sales shall have the meaning assigned to it in the licensing agreement relating to such Compound Product between Threshold and said sublicensee.

1.18 "Other Indications" means all particular cancers that are agreed in the Development Plan as the therapeutic indication for which regulatory approval will be sought in Japan after or in parallel to the First Indication.

1.19 "Parties" means Threshold and MediBIC.

1.20 "Threshold Territory" shall mean the entire world except the Asian Territory.

ARTICLE 2

DEVELOPMENT PROGRAM OVERVIEW

2.1 Overview. MediBIC shall make a payment of four million seven hundred fifty thousand U.S. dollars (US$4,750,000) to Threshold to support the development of Compound Product in the Asian Territory and in consideration of the opportunity, described herein, to derive financial benefit from the development and Commercialization of Compound Product in the Asian Territory by Threshold, its Affiliate(s), and/or sublicensee(s). The Parties shall diligently negotiate and expect to agree upon a Development Plan for Compound Products in the Asian Territory under which MediBIC, or some third party selected by Threshold, will conduct the clinical trials for the Compound Product in Japan. As consideration for its support of the development of the Compound, MediBIC will receive a percentage of Net Revenues that are received by Threshold from a sublicensee for further development and sales of Compound Products in the Asian Territory and/or a royalty on sales of Compound Products in the Asian Territory by Threshold or its Affiliate(s), as provided in Article 6. Nothing in this Agreement shall be deemed to require Threshold to continue the development or commercialization of any Compound Product(s) if Threshold determines in good faith that such development or commercialization would not be commercially practicable. In that event, Threshold will negotiate in good faith with MediBIC for a period not to exceed sixty (60) days regarding the possible sale of rights to such discontinued Compound Product(s) to MediBIC. Any sale of such rights agreed to by the parties will be set forth in a separate written agreement.

ARTICLE 3

PAYMENT TO THRESHOLD

3.1 Payment. Within thirty (30) days after the Effective Date, and subject to the terms of this Agreement as described below, MediBIC will make a payment of four million seven hundred fifty thousand U.S. dollars (US$4,750,000; the MediBIC Payment) to Threshold.

3.2 Payment Method. MediBIC shall make payment of the MediBIC Payment by bank wire transfer in immediately available funds to an account designated by Threshold.

3.3 Refund of Payment. Threshold will refund the MediBIC Payment in the event that the Parties are unable to agree, before March 1, 2005 (or such later date agreed in writing by the Parties), on a Development Plan for the Compound Product in the Asian Territory; any such refund of the MediBIC Payment shall terminate this Agreement.

ARTICLE 4

DEVELOPMENT PLAN

4.1 Overview. The Development Plan shall describe all major activities that the Parties anticipate will be necessary for the approval of a Compound Product for the First Indication in Japan by [***]. The Development Plan shall also describe manufacturing arrangements and other steps, if any, that must be taken in the Asian Territory prior to regulatory approval in Japan to provide

maximum commercial potential for the Compound Product in the Asian Territory. The Development Plan shall include, but not be limited to, the terms as described in Section 4.3.

4.2 Preparation of Development Plan. A Joint Development Committee (JDC) will be established as provided in Section 5.2 below and will meet as soon as practicable after the Effective Date to begin preparing the Development Plan.

4.3 Contents of Development Plan. The Development Plan will include, but is not necessarily limited to, the following provisions:

(a) First Indication. The choice of the First Indication will be stated in the Development Plan and will be the focus of initial clinical development activities thereunder to support regulatory approval of Compound Product in Japan.

(b) Additional Indications. The choice of Other Indications will be stated in the Development Plan and will be the focus of clinical development activities after or in parallel to, but with a lower priority than, the First Indication.

(c) Clinical Trials. The clinical trials that the Parties anticipate will be necessary to achieve regulatory approval of a Compound Product for the First Indication and a projection of the clinical trials that will be required for the Other Indications will be described in the Development Plan. Threshold expects to engage MediBIC or a third party to conduct all clinical trials for the First Indication.

(i) Timeline. The anticipated timeline for clinical trials and regulatory submissions leading to approval of a Compound Product for the First Indication shall be set forth in the Development Plan.

(ii) Parameters of the Trials. The number and location of clinical trial sites, proposed principal investigators, if any, anticipated number of subjects in each trial**,** and other such administrative parameters of the contemplated clinical trials shall be set forth in the Development Plan.

(iii) Protocol. A draft of the protocol including endpoints, to the extent they can be projected to the satisfaction of the Parties prior to March 1, 2005, for the First Indication shall be set forth in the Development Plan.

(iv) Regulatory Submissions. A description of the regulatory submissions that will be necessary, and the cost and other resources that will be necessary, to prepare and submit the necessary submissions for the First Indication shall be set forth in the Development Plan.

(v) Manufacturing Supply. A description of the anticipated source of supply of Compound Product used in the clinical trials shall be set forth in the Development Plan.

(d) Development Budget. The Development Plan shall include a Development Budget that estimates the expenses to be incurred in performing the Development Plan for the First Indication and for any Other Indications to be pursued contemporaneously therewith.

(e) Current Relationships with Japanese Pharmaceutical Companies. The Development Plan shall set forth those Japanese Pharmaceutical Companies with whom Threshold has a current relationship or has had prospective business discussions. Thereafter, the Parties agree to inform each other in writing regarding which Japanese Pharmaceutical Companies they have contacted consistent with the provisions of this Agreement. The Development Plan shall be deemed amended to include those Japanese Pharmaceutical Companies that have been contacted by either party.

4.4 Approval of the Development Plan. The Parties agree to appoint personnel, as provided in Section 5.1, to work diligently to prepare a Development Plan acceptable to both Parties before March 1, 2005. To become effective hereunder, the Development Plan must be agreed upon, as evidenced by the signatures of an authorized representative of each Party, on or before March 1, 2005. If the Parties are unable to agree on a Development Plan by that date, and unless an extension of such deadline is agreed in writing by the Parties, Threshold will refund the MediBIC Payment, as described in Sections 3.1 and 3.3, to MediBIC, and this Agreement will terminate, except for the Confidentiality obligations, which will survive, under Sections 8.1 and 8.2.

4.5 Modifications. After approval by the Parties, the Development Plan may be modified by the Parties pursuant to the authority of the JDC as established in Section 5.5, below. As provided in Section 5.5, the JDC may modify any aspect of the Development Plan, and Threshold shall have the right, in its sole discretion, to modify any aspect of the Development Plan in the event the JDC is unable to reach agreement on a matter relating to the development of Compound Product in the Asian Territory.

4.6 Regulatory Approvals. In the event the Development Plan provides for material participation by MediBIC in the development of Compound Products, MediBIC shall provide all assistance reasonably requested by Threshold in complying with all requirements of applicable laws, rules, and regulations related to regulatory filings and approvals relating to Compound Products in any country in the Asian Territory. If MediBIC is required by applicable laws or regulations of a regulatory authority having jurisdiction in the Asian Territory to disclose information directly to such regulatory authority relating to a Compound Product, MediBIC shall notify Threshold in writing of the requirement and the particulars of the information required to be disclosed, and MediBIC shall coordinate with Threshold in making any such disclosure.

ARTICLE 5

JOINT DEVELOPMENT COMMITTEE

5.1 Overview. The JDC shall work diligently to prepare a Development Plan agreeable to both Parties by March 1, 2005. Thereafter, provided the Development Plan has been agreed upon by the Parties, the JDC will manage the development activities described in the Development Plan and adjust the Development Plan as necessary to reflect new information until the MediBIC Payment has been expended. Threshold shall notify MediBIC when the MediBIC Payment has been

expended, and at that time, the JDC shall cease to exist, and Threshold shall assume responsibility to manage all development activities relating to Compound Products. The JDC will also coordinate activities with Threshold and MediBIC and be responsible for coordinating, to the extent Threshold determines such coordination necessary, the development activities of the Compound Product in the Asian Territory with development activities in the Threshold Territory.

5.2 Membership. The JDC shall be composed of at least four members, two members appointed by each Party. Each Party shall designate its initial JDC representatives at the Effective Date so the JDC may begin preparation of the Development Plan as soon as possible after the Effective Date. Each Party may replace its JDC representatives at any time upon written notice to the other Party. Threshold will designate one of its initial JDC representatives as the Chairperson of the JDC.

5.3 Meetings of the Joint Development Committee. Except for the first meeting of the JDC, which will occur as soon as practicable after the execution of this Agreement, future meetings of the JDC shall be held at such times as shall be mutually agreed upon by the Parties, but in no event less often than quarterly until Threshold has paid or otherwise incurred expenses directly relating to development of Product Compound in the Asian Territory that total to an amount that equals or exceeds the MediBIC Payment, at which point the JDC will be dissolved and cease to exist. Additional persons from each Party may attend meetings of the JDC without voting rights. Minutes of the meeting shall be confirmed by both Parties at each meeting.

5.4 Voting. The JDC will make its decisions by majority vote, with each Party's representatives collectively having one vote. If there is a deadlock in the JDC vote, then Threshold will have authority to cast an additional vote.

5.5 Responsibilities of the Joint Development Committee. The JDC shall agree on the initial Development Plan, shall exercise oversight of the implementation of the Development Plan, and shall approve all modifications and addenda to the Development Plan. To satisfy its responsibilities, the JDC shall prepare and submit to the Parties, by the first day of each calendar year, an updated Development Plan that includes a detailed description of all development anticipated to be performed during the following calendar year.

5.6 Reporting to MediBIC After Dissolution of the JDC. After the dissolution of the JDC, Threshold shall supply MediBIC annual updates within thirty (30) days of each anniversary of the Effective Date regarding development and Commercialization activities relating to Compound Products in the Asian Territory until a Compound Product is marketed in the Asian Territory, in which event, the annual update will be superseded by royalty reports, or until development is stopped based on Threshold's determination not to continue development or Commercialization of a Compound Product in the Asian Territory.

ARTICLE 6

PAYMENT TO MEDIBIC

6.1 Payments to MediBIC for Sublicensee Sales of Compound Product in the Asian Territory. If Threshold (or any successor to or Affiliate of Threshold holding commercial

rights to Compound Products) receives payments from an independent third party sublicensee based on the development and/or Commercialization of a Compound Product in the Asian Territory (i.e., upfront payments for a commercial agreement, milestone payments, or royalty on sales of a Compound Product), and such payments exceed amounts Threshold owes to third parties as a result of such activities (including, in the case of a sublicense in connection with the resolution of any patent claim or dispute, reasonable attorney's fees and expenses, and any damages or other payments, including royalties, arising therefrom) so that there are Net Revenues, then Threshold shall make payments to MediBIC on those Net Revenues as follows:

(a) [***] percent ([***]%) of the Net Revenues received by Threshold if [***];

(b) [***] percent ([***]%) of the Net Revenues received by Threshold if the sublicensee making the payments is a company other [***].

6.2 Payments to MediBIC for Sales by Threshold. In the event Threshold, as opposed to a sublicensee, directly or through a successor or Affiliate sells Compound Product in the Asian Territory, Threshold (or its successor or Affiliate) will pay MediBIC [***] percent ([***]%) of the Net Sales of the Compound Product in the Asian Territory for all sales made by Threshold or its successor or Affiliate in the Asian Territory.

6.3 Incentive Payments for Successful Sublicensing to a [***]. In the event that [***]:

(a) Threshold shall pay to MediBIC [***].

(b) Threshold shall pay to MediBIC [***].

(c) [***].

(d) [***].

6.4 Payment Method. All payments due under this Agreement to MediBIC shall be made by bank wire transfer in immediately available funds to an account designated by MediBIC. Royalties due on Net Sales or Net Revenues made in currencies other than United States dollars shall be made, at Threshold's election, either in such currencies or in United States dollars after conversion pursuant to Section 6.4(b) below. All payments, excluding the initial payment made to Threshold under Section 3.1, shall be paid within ninety (90) days after the end of each June and December. Each payment of royalties shall be accompanied by a statement of the amount of Net Sales or Net Revenues, as applicable, during such period, the amount of Net Sales or Net Revenues, as applicable, to date as of the end of such period where necessary in determination of royalty rates, and the amount of royalties due on such sales or revenue. MediBIC hereby agrees that no royalties shall be payable upon samples of the Compound Product used for the purpose of promoting such Compound Product, in such quantities as are standard in the industry for comparable products.

(a) Taxes. Any withholding of taxes levied by tax authorities on payments hereunder shall be borne by MediBIC, and deducted by Threshold from the sums otherwise payable for payment to the proper tax authorities on MediBIC's behalf. Threshold agrees to cooperate with MediBIC, at MediBIC's expense, in the event MediBIC claims exemption from such withholding or seeks deductions under any double taxation or other similar treaty or agreement from time to time in force, such cooperation to consist of providing receipts of payment of such withholding taxes imposed on payments made hereunder.

(b) Foreign Exchange. If Threshold elects to remit payment of royalties hereunder in United States Dollars on Net Sales or Net Royalties received in currencies other than United States dollars, such amounts shall be converted at the official rate of exchange of the currency of the country from which the royalties are payable, as quoted in the *Wall Street Journal* for the last business day of the calendar quarter in which the royalties are payable. If the transfer of or the conversion into the United States dollar equivalents of any such remittance in any such instance is not lawful or possible,]the payment of such part of the royalties as is necessary shall bemade by the deposit thereof, in the currency of the county where the sale was made on which the royalty was based to the credit and account of MediBIC or its nominee in any commercial bank or trust company of MediBIC's choice located in that country, prompt written notice of which shall be given by Threshold to MediBIC.

(c) Records; Audit. During the term of this Agreement and for a period of three (3) years thereafter, both Parties shall keep complete, true and accurate books of accounts and records for the purpose of determining the payments to be made under this Agreement. Such records will be open for an audit during the term of this Agreement and for the three (3) year period thereafter by U.S. independent accountants selected by MediBIC and reasonably acceptable to Threshold, solely for the purpose of verifying payment statements hereunder. Such accountants shall execute a suitable confidentiality agreement reasonably acceptable to Threshold prior to conducting such audit. Such representatives may disclose to MediBIC only their conclusions regarding the accuracy and completeness of royalty payments and of records related thereto, and shall not disclose any other information from such audit without the prior written consent of Threshold. Such inspections shall be made no more than once each calendar year, at reasonable time and on reasonable notice. Any adjustment in the amount of payments or royalties due MediBIC on account of overpayments or underpayments disclosed in such audit shall be made at the next date when royalty payments are to be made to hereunder. No claim for underpayment may be made by MediBIC more than six (6) months following completion of such audit.

ARTICLE 7

INTELLECTUAL PROPERTY RIGHTS

7.1 License to Threshold of MediBIC Know-How. MediBIC hereby grants Threshold an exclusive, royalty-free (excluding the payments and royalties provided in this Agreement) license to MediBIC Know-How to make, have made, use, offer to sell, sell and import Compound Product throughout the world.

ARTICLE 8

CONFIDENTIALITY

8.1 Confidential Information; Exceptions. During the term of this Agreement, and for a period of five (5) years after termination thereof, each Party will maintain all Confidential Information in trust and confidence and will not disclose any Confidential Information to any third party or use any Confidential Information for any purpose other than as expressly authorized under this Agreement. Each Party may use such Confidential Information only to the extent required to accomplish the purposes of this Agreement or to the extent required by law, regulation or government or judicial order. Confidential Information shall not be used for any purpose or in any manner that would constitute a violation of any laws or regulations, including without limitation the export control laws of the United States. Confidential Information shall not be reproduced in any form except as required to accomplish the intent of this Agreement. No Confidential Information shall be disclosed to any employee, agent, consultant, Affiliate, or sublicensee who does not have a need for such information. Each Party will use at least the same standard of care as it uses to protect proprietary or confidential information of its own to ensure that suchemployees, agents, consultants and clinical investigators do not disclose or make any unauthorized use of the Confidential Information. Each Party will promptly notify the other upon discovery of any unauthorized use or disclosure of the Confidential Information.

Confidential Information shall not include any information which:

(a) is now, or hereafter becomes, through no act or failure to act on the part of the receiving party, generally known or available;

(b) is known by the receiving party at the time of receiving such information, as evidenced by its records;

(c) is hereafter furnished to the receiving party by a third party, as a matter of right and without restriction on disclosure;

(d) is independently developed by the receiving party without any breach of this Agreement; or

(e) is the subject of a written permission to disclose provided by the disclosing party.

Additionally, either party may disclose Confidential Information of the other party to the extent required to comply with any court or governmental subpoena, process, order or regulation; provided, however, that the party seeking to make such disclosure shall promptly notify the other party to provide it an opportunity to seek to challenge or limit the scope of such disclosure.

8.2 Financial Terms. The Parties agree that the financial terms of the Agreement will be considered Confidential Information of both parties. Notwithstanding the foregoing, Threshold may disclose such terms to *bona fide* potential sublicensees, and either Party may disclose such terms in connection with financing efforts. In connection with any such disclosure, each Party agrees to request confidential treatment of such information. Threshold and MediBIC shall have the further right to disclose the terms of the Agreement to any potential acquirer, merger partner, or other *bona fide* potential financial partner, subject to a requirement to seek confidential treatment of such information.

ARTICLE 9

TERM AND TERMINATION OF AGREEMENT

9.1 Failure to Reach a Development Plan. This Agreement shall expire on March 1, 2005 if a Development Plan has not been agreed upon by the Parties, or if the Parties have not extended such deadline in writing, and the MediBIC Payment will be refunded to MediBIC pursuant to Section 3.3 of this Agreement.

9.2 Term. If the Parties have agreed upon a Development Plan prior to March 1, 2005 (or such later date agreed by the Parties), this Agreement will expire on the expiration date of the last to expire patent in a country in the Asian Territory that is owned or controlled by Thresholdthat claims the Compound, a Compound Product sold in such country, a process employed in such country to make the Compound or a Compound Product, or an approved use of a Compound Product in such country.

9.3 Extension. The Parties may extend the term of this Agreement by the written agreement of both Parties.

9.4 Early Termination by Threshold. If this Agreement is not terminated for failure of the Parties to agree upon on a Development Plan, Threshold may terminate this Agreement after the Development Agreement is agreed upon at any time and terminate its payment obligations under Article 6, following the written notice to MediBIC and receipt by MediBIC of the payment due it under the following schedule:

(a) Five million two hundred fifty thousand U.S. dollars (US$5,250,000) if the notice of termination is delivered to MediBIC after the Development Plan has been agreed by the Parties, but prior to the Initiation of Phase I clinical testing of a Compound Product in Japan;

(b) [***] U.S. dollars (US$[***]) if the notice of termination is delivered to MediBIC after the Initiation of Phase I clinical testing in Japan, but prior to the Initiation of Phase II clinical testing of a Compound Product in Japan;

(c) [***] U.S. dollars (US$[***]) if the notice of termination is delivered to MediBIC after the Initiation of Phase II clinical testing in Japan, but prior to the Initiation of Phase III clinical testing of a Compound Product in Japan; and

(d) Fifteen million U.S. dollars (US$15,000,000) if the notice of termination is delivered to MediBIC after the Initiation of Phase III clinical testing in Japan, but prior to regulatory approval of a Compound Product in Japan.

9.5 Accrued Rights, Surviving Obligations. Upon any expiration or termination of this Agreement, all royalty and other payment obligations hereunder shall terminate, except for any accrued rights and obligations of either Party prior to the date of such expiration or termination; provided, however, that in the case of any termination by Threshold under Section 9.4, MediBIC shall not be entitled to any accrued rights to receive payments pursuant to Article 6.

ARTICLE 10

INDEMNITY

10.1 Compound Product Liability Indemnity by Threshold. Threshold shall defend, indemnify and hold MediBIC harmless from and against all claims and expenses, including reasonable attorneys' fees, arising out of the death of or bodily injury to any person or persons resulting from the Commercialization of Compound Products by Threshold and its sublicensees, other than those claims and expenses arising from MediBIC's negligence or willful misconduct or failure to follow the Development Plan; and provided that (i) MediBIC provides Threshold prompt notice of any such claim, (ii) Threshold shall not be obligated to indemnify MediBIC for any loss in connection with any settlement unless Threshold consents in writing to such settlement, and (iii) Threshold shall have the exclusive right to defend any such claim.

ARTICLE 11

REPRESENTATIONS AND WARRANTIES

11.1 MediBIC Representations, Warranties and Indemnities. MediBIC represents and warrants the following:

(a) Corporate Authority. MediBIC is a corporation duly organized, validly existing and in good standing under the laws of Japan, has the power and authority, corporate and otherwise, to execute and deliver this Agreement and to perform its obligations hereunder and thereunder, and has by all necessary corporate action duly and validly authorized the execution and delivery of this Agreement, and the performance of its obligations hereunder.

(b) Binding Obligation. This Agreement is the valid and legally binding obligation of MediBIC in accordance with its terms, subject to bankruptcy, reorganization, insolvency, moratorium and similar laws and to general principles of equity which are within the discretion of courts of applicable jurisdiction.

(c) No Conflicts. The execution, delivery and performance by MediBIC of this Agreement, and each other agreement, document, or instrument now or hereafter executed and delivered by MediBIC pursuant thereto or in connection herewith will not: (i) conflict with or violate the articles of incorporation or by-laws of MediBIC or any provision of any law, rule, regulation, authorization or judgment of any governmental authority having applicability to MediBIC or its actions; or (ii) conflict with or result in any breach of, or constitute a default under, any note, security agreement, commitment, contract or other agreement, instrument or undertaking to which MediBIC is a party or by which any of its property is bound.

(d) Agreements with Employees and Consultants. MediBIC has and will maintain with all MediBIC employees, agents and consultants, written agreements sufficient to enable MediBIC to perform its obligations under this Agreement, whenever MediBIC thinks it is necessary.

11.2 Threshold Representations, Warranties and Indemnities. Threshold represents and warrants the following:

(a) Corporate Authority. Threshold is a corporation duly organized, validly existing and in good standing under the laws of the state of Delaware, has the power and authority, corporate and otherwise, to execute and deliver this Agreement, and to perform its obligations hereunder, and has by all necessary corporate action duly and validly authorized the execution and delivery of this Agreement, and the performance of its obligations hereunder.

(b) Binding Obligation. This Agreement is the valid and legally binding obligation of Threshold in accordance with its terms, subject to bankruptcy, reorganization, insolvency, moratorium and similar laws and to general principles of equity which are within the discretion of courts of applicable jurisdiction.

(c) No Conflicts. The execution, delivery and performance by Threshold of this Agreement, and each other agreement, document, or instrument now or hereafter executed and delivered by Threshold pursuant thereto or in connection herewith will not: (i) conflict with or violate the articles of incorporation or by-laws of Threshold or any provision of any law, rule, regulation, authorization or judgment of any governmental authority having applicability to

Threshold or its actions; or (ii) conflict with or result in any breach of, or constitute a default under, any note, security agreement, commitment, contract or other agreement, instrument or undertaking to which Threshold is a party or by which any of its property is bound.

(d) Agreements with Employees and Consultants. Threshold has and will maintain with all Threshold employees, agents and consultants, written agreements sufficient to enable Threshold to perform its obligations under this Agreement, whenever Threshold thinks it is necessary.

11.3 Disclaimer of Warranties. EXCEPT AS EXPRESSLY SET FORTH IN THIS ARTICLE 11, NEITHER PARTY MAKES ANY REPRESENTATIONS OR WARRANTIES OF ANY KIND HEREUNDER, WITH RESPECT TO ANY PATENT RIGHTS, TECHNOLOGY, COMPOUNDS OR CONFIDENTIAL INFORMATION, INCLUDING BUT NOT LIMITED TO WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OF ANY PATENT RIGHTS OR TECHNOLOGY, OR THE NON-INFRINGEMENT OF ANY THIRD PARTY PATENTS OR PROPRIETARY RIGHTS.

ARTICLE 12

IMPORT AND EXPORT CONTROLS

12.1 United States Laws. The Parties understand and acknowledge that each of them is subject to regulation by agencies of the U.S. government, including the U.S. Department of Commerce, which prohibit export or diversion of certain products and technology to certain countries. Any and all obligations of MediBIC or Threshold to provide access to or license any technology pursuant to this Agreement, as well as any technical assistance shall be subject in all respects to such United States laws and regulations as shall from time to time govern the license and delivery of technology and products abroad by persons subject to the Jurisdiction of the United States, including the Export Administration Act of 1979, as amended, any successor or interim controlling legislation, and the Export Administration Regulations issued by the Department of Commerce, International Trade Administration, Bureau of Export Administration. Both Parties also agree to comply with the requirements of the U.S. Foreign Corrupt Practices Act (the "Act") and shall refrain from any payments to third parties which would cause MediBIC or Threshold to violate the Act. At MediBIC's request and expense, Threshold shall advise MediBIC regarding compliance with the Act.

12.2 Non-United States Laws. MediBIC and Threshold shall each provide the other Party with such reasonable assistance as may be required for the Party requesting such assistance, and at the requesting Party's expense, to comply with all non-United States laws, ordinances, rules,regulations and the like of all governmental units or agencies within any territory having jurisdiction pertaining to this Agreement, including without limitation, obtaining all import, export and other permits, certificates, licenses or the like required by such non-United States laws, ordinances, rules, regulations and the like, necessary to permit the Parties to perform hereunder and to exercise their respective rights hereunder.

ARTICLE 13

LIMITATIONS OF LIABILITY

NEITHER THRESHOLD NOR MEDIBIC WILL BE LIABLE OR OBLIGATED IN ANY MANNER FOR ANY SPECIAL INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, UNDER ANY CAUSE OF ACTION, WHETHER IN CONTRACT, TORT (INCLUDING NEGLIGENCE) STRICT LIABILITY OR OTHERWISE, AND EVEN IF INFORMED OF THE POSSIBILITY THEREOF IN ADVANCE, ARISING OUT OF THIS AGREEMENT OR BY REASON OF BREACH OF THIS AGREEMENT. THESE LIMITATIONS WILL APPLY NOTWITHSTANDING ANY FAILURE OF ESSENTIAL PURPOSE OF ANY LIMITED REMEDY HEREIN.

ARTICLE 14

MISCELLANEOUS PROVISIONS

14.1 Waiver. No waiver by either Party hereto of any breach or default of any of the covenants or agreements herein set forth shall be deemed a waiver as to any subsequent or similar breach or default.

14.2 Assignment. This Agreement shall be binding upon and inure to the benefit of the Parties hereto and their permitted successors and assigns; provided, however, that neither Party shall assign any of its rights and obligations hereunder without the prior written consent of the other party, except that no consent shall be required for any assignment incident to the merger, consolidation, reorganization, or acquisition of stock or assets affecting substantially all of the assets to which this Agreement pertains or actual voting control of the assigning Party.

14.3 Notices. Any notice or other communication required or permitted to be given to either Party hereto shall be in writing and shall be deemed to have been properly given and to be effective on the date of delivery if delivered in person or by facsimile or five (5) days after mailing by registered or certified mail, postage paid, to the other Party at the following address:

In the case of Threshold:	Threshold Pharmaceuticals, Inc. 951 Gateway Blvd. S. San Francisco, CA 94080 Attention: CEO
In the case of MediBIC:	MediBIC Co., Ltd., Daido Seimei Kasumigaseki Building 8F 1-4-2 Kasumigaseki, Chiyoda-ku, Tokyo, 100-0013 Japan Attention: CEO

Either Party may change its address for communications by a notice to the other Party in accordance with this section.

14.4 Headings. The headings of the several sections are inserted for convenience of reference only and are not intended to be a part of or to affect the meaning or interpretation of this Agreement.

14.5 Amendment. No amendment or modification hereof shall be valid or binding upon the Parties unless made in writing and signed by both Parties.

14.6 Construction of Agreement and Choice of Law, Jurisdiction and Venue. This agreement and its terms and conditions shall be governed exclusively by and construed according to the laws of California, U.S.A., excluding its choice of law provisions and also excluding the United Nations Convention on Contracts for International Sale of Goods. The official text of this Agreement and any notices given or accounts or statements required hereby shall be in English. In the event of any dispute concerning the construction or meaning of this Agreement, reference shall be made only to this Agreement as written in English and not to any other translation into any other language. All disputes which may arise between the Parties hereto in relation to the interpretation or administration of this Agreement shall be first referred to the JDC for resolution. Any disputes which the JDC shall be unable to resolve within a reasonable period of time shall be resolved by the agreement of the Chief Executive Officers of the respective Parties or their delegates. Any disputes which cannot be resolved in this manner shall be finally resolved in the courts in San Francisco, California.

14.7 Force Majeure. Any delays in performance by any Party under this Agreement (other than the payment of money) shall not be considered a breach of this Agreement if and to the extent caused by occurrences beyond the reasonable control of the Party affected, including but not limited to acts of God, embargoes, governmental restrictions, strikes or other concerted acts of workers, fire, flood, explosion, riots, wars, civil disorder, rebellion or sabotage (a "Force Majeure"). The Party suffering such occurrence shall immediately notify the other Party and any time for performance hereunder shall be extended by the actual time of delay caused by the occurrence; provided, however, that if a Party is affected by a Force Majeure event for more than ninety (90) days, the party not affected shall be entitled to terminate this Agreement with no further obligation hereunder.

14.8 Independent Contractors. In making and performing this Agreement, MediBIC and Threshold act and shall act all times as independent contractors and nothing contained in this Agreement shall be construed or implied to create an agency, partnership or employer and employee relationship between Threshold and MediBIC. At no time shall one Party make commitments or incur any charges or expenses for or in the name of the other Party.

14.9 Severability. If any term, condition or provision of this Agreement is held to be unenforceable for any reason, it shall, if possible, be interpreted rather than voided to achieve the intent of the Parties to this Agreement to the extent possible. In any event, all other terms, conditions and provisions of this Agreement shall be deemed valid and enforceable to the full extent.

14.10 Cumulative Rights. The rights, powers and remedies hereunder shall be in addition to, and not in limitation of all rights, powers and remedies provided at law or in equity, or under any other agreement between the Parties. All of such rights, powers and remedies shall be cumulative, and may be exercised successively or cumulatively.

14.11 Entire Agreement. This Agreement, and any and all Exhibits referred to herein, embodies the entire understanding of the Parties with respect to the subject matter hereof and shall supersede all previous communications, representations or understandings, either oral or written, between the Parties relating to the subject matter hereof.

IN WITNESS WHEREOF, both MediBIC and Threshold have executed this Agreement, in duplicate originals, by their respective officers hereunto duly authorized, as of the day and year hereinabove written.

THRESHOLD PHARMACEUTICAL, INC.

By: /s/ Harold E. Selick
Harold E. Selick
Title: Chief Executive Officer
Date: December 2, 2004

MEDIBIC CO., LTD.

By: /s/ Yasuhiro Hashimoto
Yasuhiro Hashimoto, MD
Title: President and CEO
Date: December 2, 2004

ADDENDUM

Side letter to Development Agreement between Threshold Pharmaceuticals and MediBIC.

Addressed To: Barry Selick, CEO of Threshold
From: Yas Hashimoto, CEO of MediBIC

Threshold and MediBIC will soon begin preparing a Development Plan for the clinical development of glufosfamide in the Asian Territory, as called for and defined in the Development Agreement between the Parties effective December 2, 2004 ("Agreement"). This letter describes certain exclusive negotiation obligations of Threshold, as set forth below, that shall be deemed part of the Agreement.

If the Parties approve the Development Plan by March 1, 2005, they will then begin good faith negotiations regarding the specifics of commercial development of products containing glufosfamide in the Asian Territory, including clinical testing and regulatory approval. In connection with such negotiations, Threshold agrees that it will not offer any other party the rights to develop and market glufosfamide in the Asian Territory for the time period described below, unless MediBIC gives prior written approval (the "MediBIC Option"). The term of this option shall commence on the date of this letter and continue until July 1, 2005 (or, earlier, if any termination of the Agreement)(the "Option Period"). The Parties may, at any time, agree in writing to extend the Option Period beyond such date.

The MediBIC Option is subject to the following limitations: During the Option Period, Threshold may negotiate with third parties regarding the development and marketing of products containing glufosfamide (a) in connection with any transaction or arrangement involving the sale or transfer of all of Threshold's stock, assets or business involving glufosfamide, whether by sale, merger, consolidation or otherwise, (b) in connection with a license agreement covering worldwide rights to develop and market products containing glufosfamide, or (c) in connection with a Japanese Pharmaceutical Company described in Section 4.3 of the Agreement.

In consideration for Threshold granting the MediBIC Option, by December 15, 2004, MediBIC will pay Threshold an amount not less than two hundred fifty thousand United States dollars (US$250,000), as agreed upon in writing by the Parties (the "Option Payment"). The Option Payment will be returned in full to MediBIC by Threshold if the Parties do not approve the Development Plan prior to March 1, 2005, or if during the Option Period, (a) Threshold consummates any transaction transferring its glufosfamide assets to a third party, (b) enters into a worldwide license agreement for the development of glufosfamide, or (c) enters into a transaction or arrangement for glufosfamide with a Japanese Pharmaceutical Company other than one that satisfies the requirements of Section 6.1(a) of the Agreement. In addition, at any time during the Option Period, Threshold may return the Option Payment in full to MediBIC and be released from the MediBIC Option.

IN WITNESS WHEREOF, both MediBIC and Threshold have executed this Agreement, in duplicate originals, by their respective officers hereunto duly authorized, as of the day and year hereinabove written.

THRESHOLD PHARMACEUTICAL, INC.

By: /s/ Harold E. Selick
Harold E. Selick
Title: Chief Executive Officer
Date: December 2, 2004

MEDIBIC CO., LTD.

By: /s/ Yasuhiro Hashimoto
Yasuhiro Hashimoto, MD
Title: President and CEO
Date: December 2, 2004

Exhibit 10.18

Yasuhiro Hashimoto, M.D.
President and CEO
MediBIC Co., Ltd.
Daido Seimei Kasumigaseki Building 8F
1-4-2 Kasumigaseki, Chiyoda-ku
Tokyo 100-0013 Japan

Re: Development Agreement between Threshold Pharmaceuticals, Inc., and MediBIC Co., Ltd.

Dear Yas,

I am writing you in regard to the Development Agreement between our companies having an Effective Date of 30 November 2004 and its accompanying side letter, both signed 2 December 2004. This letter confirms our understanding that, pursuant to the Development Agreement and side letter, Threshold has granted and hereby confirms its grant to MediBic of a non-exclusive license to use Threshold confidential information relating to glufosfamide for the limited purpose of preparing the Development Plan and any associated marketing plans as authorized under the Development Agreement, and if such Development Plan is agreed upon by the parties, this non-exclusive license to use Threshold confidential information shall continue for the time necessary for MediBIC to perform its obligations under the Development Plan.

In addition, this letter amends the Development Agreement to remove North Korea from the list of countries in the "Asian Territory" as defined in Section 1.3.

Please acknowledge your receipt of this letter and agreement by signing and returning one of the two duplicate originals provided to you.

Best regards,

/s/ HAROLD E. SELICK
Harold E. Selick
Chief Executive Officer
Threshold Pharmaceuticals, Inc.

ACCEPTED AND AGREED

/s/ YASUHIRO HASHIMOTO
Yasuhiro Hashimoto, M.D.
President and CEO
MediBIC Co., Ltd

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the use in this Amendment No. 6 to Registration Statement on Form S-1 of our report dated April 8, 2004, except as to Note 12 which is as of January 26, 2005, 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
January 26, 2005