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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2004

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number: 000-51136

THRESHOLD PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**94-3409596**
(State or other jurisdiction of incorporation or organization)	**(IRS employer Identification number)**
1300 Seaport Boulevard, Redwood City, CA	**94063**
(Address of principal executive office)	**(Zip Code)**

(650) 474-8200
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) if the Act: None
Securities registered pursuant to Section 12(g) of the act: Common Stock, $0.001 par value
(Title of Class)

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. Yes ☒ No ☐

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Exchange Act. Yes ☐ No ☒

The aggregate market value of the voting stock held by non-affiliates of the Registrant based on the last sale price for such stock on June 30, 2004: Not applicable because trading of the registrant's common stock on the Nasdaq National Market did not commence until February 4, 2005.

Documents incorporated by reference: Portions of the Proxy Statement for Registrant's Annual Meeting of Shareholders to be held May 19, 2005 (the Proxy Statement), are incorporated herein by reference into Part III.

Threshold Pharmaceuticals, Inc.
TABLE OF CONTENTS

		Page
	Part I	3
Item 1.	Business	3
Item 2.	Properties	25
Item 3.	Legal Proceedings	25
Item 4.	Submission of Matters to a Vote of Security Holders	25
	Part II	26
Item 5.	Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	26
Item 6.	Selected Financial Data	27
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	28
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	53
Item 8.	Financial Statements and Supplementary Data	55
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	75
Item 9A.	Controls and Procedures	76
Item 9B.	Other Information	76
	Part III	77
Item 10.	Directors and Executive Officers of the Registrant	77
Item 11.	Executive Compensation	77
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	77
Item 13.	Certain Relationships and Related Party Transactions	77
Item 14.	Principal Accountant Fees and Services	77
	Part IV	78
Item 15.	Exhibits and Financial Statement Schedules	78
	Signatures	80

PART I

This annual report on Form 10-K, including the sections entitled "Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations," 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," "may," or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements may include statements regarding:

- 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 active pharmaceutical ingredients (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 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 Form 10-K under the caption "Risk Factors." You should read these factors and the other cautionary statements made in this Form 10-K as being applicable to all related forward-looking statements wherever they appear in this Form 10-K. 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. Unless the context requires otherwise, in this Form 10-K 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 Form 10-K are the property of their respective owners.

ITEM I. BUSINESS

Overview

Threshold Pharmaceuticals, Inc, a biotechnology company incorporated in Delaware in 2001, is 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 and hyperplastic cells and that 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. (1) 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. (2) TH-070 (lonidamine), our lead product candidate for the treatment of symptomatic BPH, has completed enrollment in a Phase 2 clinical trial, and we have completed an evaluation of the interim data. We plan to initiate a Phase 3 clinical trial in several European countries and a Phase 2 clinical trial in the US for TH-070 to treat symptomatic BPH beginning mid-2005. (3) 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 estimated that 563,700 people would die from cancer in the United States in 2004. Many advanced or metastatic cancers, such as pancreatic, 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 therapies have significant side effects and are not completely effective. 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 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. 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 low oxygen, or 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 which causes an enlargement of the prostate 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 that TH-070 treats the underlying condition by reducing prostate size and treating the symptoms of BPH.

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 evaluated	Initiate Phase 3 EU trial mid-2005 Initiate Phase 2 US trial mid-2005
2-Deoxyglucose (2DG)		
• Various solid tumors	Phase 1 in progress	Initial data by 4Q05

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 and other indications.

Glufosfamide combines glucose with the active part of an approved alkylator, a member of a widely used class of chemotherapy drugs. 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 estimated that 31,860 patients would be diagnosed with pancreatic cancer in the United States in 2004, and approximately 31,270 patients would 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 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 trial design calls 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 24 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 30 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 at least one other indication. 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 (lonidamine)

TH-070 (lonidamine), 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 have evaluated interim clinical data from a Phase 2 trial of TH-070 for the treatment of symptomatic BPH. We plan to initiate a Phase 3 trial in several European countries and a Phase 2 trial in the US for this indication by mid-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 urinary 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. 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 was 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 Phase 3 trial in several European countries and a Phase 2 trial in the US for TH-070 to treat symptomatic BPH in mid-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	–11.2%	+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. We plan to initiate a Phase 3 trial in several European countries and a Phase 2 trial in the US of TH-070 for the treatment of symptomatic BPH mid-2005. Our Phase 3 European trial will be a multicenter, randomized, double-blinded, placebo-controlled study and our Phase 2 US trial will be a multicenter, randomized and placebo-controlled dose-comparison study. These trials will measure the same variables we measured in our Phase 2 open label trial. We believe there will be at least one additional Phase 3 trial prior to seeking regulatory approval in the US.

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 are also considering 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 these data support 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 fourth 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 a lead indication for our Phase 2 program based on the results of the ongoing Phase 1 trial.

We are also considering additional trials such as a second Phase 1 trial of a single dose of 2DG in patients with prostate cancer. This study would evaluate the biological effect of 2DG on metabolism in the prostate and 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 evaluated interim data from a Phase 2 trial for the treatment of symptomatic BPH and plan to begin a Phase 3 trial in several European countries and a Phase 2 trial in the US for the treatment of symptomatic BPH in mid-2005. For 2DG, we have an ongoing Phase 1 trial to evaluate the safety, blood levels and maximum tolerated dose in patients with solid tumors. We intend to advance all of our clinical programs as aggressively as possible, and assuming clinical results are positive, expect to file NDAs with the FDA and other foreign regulatory agencies for glufosfamide in 2007 and TH-070 in 2008. 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 and seek strategic collaborations in other 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 three years; however, should our current supply not remain stable and our alternate suppliers not be able to provide material, 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 but not yet received additional TH-070 API from Jiangsu Hengrui Medicine Company, Ltd. We have an agreement with Pharmaceutics International, Incorporated (PII) for the supply of clinical lots of TH-070 drug product. We have received, enough drug product supply that has been tested and released by PII for our planned Phase 3 European BPH trial and have received drug product supply tested by PII for the planned Phase 2 US BPH trial. 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 plan to 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 preclinical 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 worldwide 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 June 15, 2005. 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 June 15, 2005. 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 December 31, 2004, we owned 23 pending US patent applications and six international (PCT) patent applications and 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 two United States provisional patent applications describing the use of glufosfamide in combination with other agents, including 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 seven 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 five provisional United States patent applications 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. Tarceva, under development by OSI Pharmaceuticals, Genentech and Roche, met its primary endpoint in a Phase 3 combination trial with gemcitabine 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:

- preclinical 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.

Employees

As of December 31, 2004 we had 42 employees, including 15 who hold Ph.D. and/or M.D. degrees. 29 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.

Executive Officers of the Registrant

The following table sets forth, as of December 31, 2004, information about our executive officers.

Name	Age	Position(s)
Executive Officers		
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, M.D., M.P.H.	42	Chief Medical Officer
Significant Employee		
Mark G. Matteucci, Ph.D.	50	Vice President of Discovery

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.

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.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy information and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

You may obtain a free copy of our annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website on the World Wide Web at http://www.thresholdpharm.com or by contacting the Investor Relations Department at our corporate offices by calling 650-474-8200.

ITEM 2. PROPERTIES

We sublease approximately 33,700 square feet of laboratory and office space in Redwood City, California, under an agreement that terminates in February 2010. We believe these facilities are suitable and adequate for our current needs.

ITEM 3. LEGAL PROCEEDINGS

We are not currently involved in any legal proceedings that could have a material impact on our business or financial condition. The company is subject to various routine claims and legal proceedings that arise in the ordinary course of business.

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

No matters were submitted to a vote for our stockholders, through solicitation of proxies or otherwise, in the fourth quarter of fiscal year 2004.

PART II

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

Our common stock is quoted on the Nasdaq National Market under the symbol "THLD" and has been quoted since our initial public offering on February 4, 2005. Prior to such date there was no public market for our common stock.

Holders

As of March 23, 2005 there were approximately 123 stockholders of record of Threshold common stock.

Dividends

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.

Recent Sales of Unregistered Securities

During the year ended December 31, 2004, we issued to employees, directors and consultants 3,518,304 shares of common stock upon the exercise of stock options at a weighted average exercise price of $0.25 per share. During the same period, we granted options to purchase 2,222,333 shares of common stock at a weighted average exercise price of $0.36 per share.

The issuances described above were deemed exempt from registration under the Securities Act in reliance on Rule 701 promulgated thereunder as transactions pursuant to compensatory benefit plans and contracts relating to compensation. The recipients of securities in each such transaction represented their intention to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the share certificates and other instruments issued in such transactions. All recipients either received adequate information about the Company or had access, through employment or other relationships, to such information.

There were no underwriters employed in connection with any of the transactions set forth above in this Item 5.

Use of Proceeds From Registered Securities

We registered shares of our common stock in connection with our initial public offering under the Securities Act of 1933, as amended. Our Registration Statement on Form S-1 (Reg. No. 333-114376) in connection with our initial public offering was declared effective by the SEC on February 3, 2005. The offering commenced as of February 4, 2005. The offering did not terminate before any securities were sold. As of the date of the filing of this report, the offering has terminated and 6,112,601 shares of our common stock registered were sold. The underwriters of the offering were Banc of America Securities LLC, CIBC World Markets Corp, Lazard Freres & Co. LLC and William Blair & Company, LLC.

All 6,112,601 shares of our common stock registered in the offering were sold at the initial public offering price per share of $7.00. The aggregate purchase price of the offering was approximately $42.8 million. The net offering proceeds to us after deducting total expenses were $37.9 million. We incurred total estimated expenses including the underwriters' discount in connection with the offering of $4.9 million. No payments for such expenses were made directly or indirectly to (i) any of our directors, officers or their associates, (ii) any person(s) owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

The net offering proceeds have been invested in short-term investment-grade securities.

There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b).

ITEM. 6 SELECTED FINANCIAL DATA

We are a development stage company. The following selected statement of operations data for the years ended December 31, 2004, 2003, and 2002 and balance sheet data as of December 31, 2004 and 2003 have been derived from our audited financial statements included elsewhere in this Form 10-K. The following selected statement of operations data for the period from October 17, 2001 (inception) to December 31, 2001 and balance sheet data as of December 31, 2002 and 2001 are derived from our audited financial statements not included in this Form 10-K. The selected financial data set forth below have been prepared in accordance with accounting principles generally accepted in the United States of America and should be read together with our 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 Form 10-K.

	Years Ended December 31,			Period from October 17, 2001 (date of inception) to December 31, 2001
	2004	2003	2002	
	(In thousands, except per share data)			
Operating expenses:				
Research and development (1)	$ 16,327	$ 6,252	$ 2,179	$ 35
General and administrative (1)	7,649	2,057	306	201
Total operating expenses	23,976	8,309	2,485	236
Loss from operations	(23,976)	(8,309)	(2,485)	(236)
Interest income	443	65	27	—
Interest expense	(33)	(59)	—	—
Net loss	(23,566)	(8,303)	(2,458)	(236)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	(40,862)	—	—
Net loss attributable to common stockholders	$(23,566)	$(49,165)	$(2,458)	$ (236)
Net loss per common share:				
Basic and diluted	$ (20.25)	$(501.68)	$(34.62)	$ (2.13)
Weighted average number of shares used in per common share calculations:				
Basic and diluted	1,164	98	71	111
(1) Includes non-cash stock based compensation of:				
Research and Development (Employee)	$ 2,279	$ 57	$ —	$ —
Research and Development (Non-Employee)	681	256	21	—
General and Administrative	3,015	753	1	—
Total non-cash stock-based compensation	$ 5,975	$ 1,066	$ 22	$ —

	As of December 31,			
	2004	2003	2002	2001
	(In thousands)			
Balance Sheet Data:				
Cash and cash equivalents	$ 14,339	$40,609	$ 6,215	$ 187
Marketable Securities	14,326	209	45	—
Working capital	21,967	40,177	6,154	2
Total assets	32,213	41,270	6,726	195
Notes payable, less current portion	382	242	—	—
Redeemable convertible preferred stock	49,839	49,839	8,977	236
Total stockholders' deficit	(26,473)	(9,695)	(2,667)	(234)

We completed our initial public offering in February 2005 selling 5,333,333 shares of common stock for net proceeds of approximately $32.8 million. In addition, we received net proceeds of $5.1 million from the exercise of 779,268 shares of the underwriters' over-allotment. All shares of redeemable convertible preferred stock converted into 20,552,815 shares of common stock upon the completion of the offering.

ITEM 7. 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 Form 10-K.

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 Form 10-K. 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 and diseased 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 (BPH). We have three product candidates. (1) 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. (2) TH-070, our lead product candidate for the treatment of symptomatic BPH, has completed enrollment in a Phase 2 clinical trial, which commenced in the first quarter of 2004, and we have evaluated interim data. We plan to initiate, in mid-2005, a Phase 3 trial in several European countries and a Phase 2 trial in the US for TH-070 to treat symptomatic BPH. (3) 2-deoxyglucose, or 2DG, is for the treatment of solid tumors and 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 will specifically target 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 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, through December 2004, we have funded our operations primarily through the private placement of equity securities. We have incurred a loss from operations for the year ended December 31, 2004 of $24.0 million and cumulative losses from operations since our inception through December 31, 2004 of $35.0 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 our Phase 3 and Phase 2 trials for TH-070 for the treatment of symptomatic BPH in mid-2005. These clinical trials will involve a greater number of patients, will be conducted at multiple sites and in several countries, will be 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, business development, commercial operations and administrative 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 several years.

Research and Development Expenses

Research and development expenses consist primarily of costs of conducting clinical trials, salaries and related costs for personnel including non-cash stock-based compensation, costs of clinical materials, costs for research projects and preclinical studies, costs related to regulatory filings, and facility costs. Contracting and consulting expenses are a significant component of our research and development expenses as we rely on expert consultants and contractors in many of the areas mentioned above. We recognize expenses as they are incurred. Our accruals for expenses associated with preclinical and clinical studies and contracts associated with clinical materials 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 December 31, 2004, we spent an aggregate of $24.8 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 and recruiting. 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 December 31, 2004, we spent an aggregate of $10.2 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 our initial public offering which was completed in February 2005, we 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 $20.4 million for the year ended December 31, 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, 2004 was $5.3 million, for the year ended December 31, 2003 was $0.8 million, and $1,000 for the year ended December 31, 2002. Assuming no forfeitures, we expect the remaining $16.6 million to be amortized as follows: $5.3 million for the year ending December 31, 2005, $5.0 million for the year ending December 31, 2006, $4.7 million for the year ending December 31, 2007, and $1.6 million for the year ending December 31, 2008.

During May 2004, we granted options with a cancellation provision to purchase 386,778 shares of common stock to employees which required variable accounting. The measurement of stock-based compensation for these options was subject to periodic adjustment resulting from changes in the fair value of our common stock. The cancellation provision of these options was eliminated in December 2004, and no longer requires variable accounting. We recognized $2.4 million in stock-based compensation expense in 2004 for these options under variable accounting included in the amounts above.

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 toOther 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 $0.7 million, $0.3 million and $21,000 of stock-based compensation expense during the years ended December 31, 2004, 2003 and 2002, respectively.

Results of Operations for the Years Ended December 31, 2004 and 2003

Research and Development

Research and development expenses for the year ended December 31, 2004 were $16.3 million compared to $6.3 million for the year ended December 31, 2003. The $10.0 million increase in research and development expenses was due primarily to increases of $2.5 million for clinical trial costs, $1.9 for increased staffing, $1.5 million for licensing costs, $0.9 million for clinical drug supply, $0.3 million for facility and related costs and $2.6 million for non-cash stock-based compensation.

Research and development expenses associated with glufosfamide were $7.5 million for the year ended December 31, 2004 and were $0.1 million for the year ended December 31, 2003. This increase was due to the activities leading up to and initiation in 2004 of a Phase 3 clinical trial for the second-line treatment of pancreatic cancer. Research and development expenses associated with TH-070 increased to $3.3 million for the year ended December 31, 2004 from $0.4 million for the year ended December 31, 2003 due to the Phase 2 trial conducted in 2004. Research and development expenses associated with 2DG were $2.8 million for the year ended December 31, 2004 and were $4.2 million for the year ended December 31, 2003. This decrease is a result of the completion of a major portion of preclinical studies during 2003. Discovery research expenses were approximately $2.7 million for the year ended December 31, 2004 and were $1.6 million for the year ended December 31, 2003. The increase in discovery research expenses was primarily due to increased staffing. We expect our research and development expenses to increase in 2005 as we continue our Phase 3 trial for glufosfamide for the second-line treatment of pancreatic cancer and our Phase 1/2 trial for glufosfamide in combination with Gemzar for the first-line treatment of pancreatic cancer, and initiate a European Phase 3 trial and a US Phase 2 trial for TH-070 for the treatment of symptomatic BPH in mid-2005.

General and Administrative

General and administrative expenses for the year ended December 31, 2004 were $7.6 million versus $2.1 million for the year ended December 31, 2003. The $5.5 million increase in general and administrative expenses was primarily due to $1.6 million for increased staffing, $0.7 million from increased spending on patent, legal, and audit services, $0.5 million from other services, primarily public relations, $0.3 million from increased facility and related costs, and $2.3 million from non-cash stock-based compensation. We expect our general and administrative expenses to increase in 2005 due to an increase in personnel and patent expenses and the costs of compliance with laws and regulations applicable to a public company, including compliance with Section 404 of the Sarbanes-Oxley Act of 2002.

Interest Income (Expense)

Interest income for the year ended December 31, 2004 was $443,000 compared to $65,000 for the year ended December 31, 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 year ended December 31, 2004 was $33,000 compared to $59,000 for the year ended December 31, 2003. The decrease in interest expense was primarily the result of the amortization, in 2003, of debt issuance costs associated with warrants issued in conjunction with our 2003 line of credit.

Results of Operations for the Years Ended December 31, 2003 and 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 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.

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.

Interest expense was $59,000 for the year ended December 31, 2003 which consists of interest expense 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.

Income Taxes

We incurred net operating losses for the years ended December 31, 2004, 2003, and 2002 and the period ended December 31, 2001 and, accordingly, we did not pay any federal or state income taxes. As of December 31, 2004, we had accumulated approximately $23.8 million and $23.8 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 begin to expire in 2022 and 2014, for federal and state tax purposes, 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.

At December 31, 2004, we had research credit carryforwards of approximately $0.5 million and $0.6 million for federal and California state income tax purposes, respectively. If not utilized, the federal carryforwards will expire in various amounts beginning in 2022. The California state research credit can be carried forward indefinitely.

We have not recorded a benefit from our net operating loss or research credit 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.

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 December 31, 2004, of $34.6 million. We have not generated any revenues and do not expect to generate revenue from product candidates for several years. From inception until our initial public offering in February 2005 we 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. In February 2005 we completed our initial public offering of 5,333,333 shares of common stock at $7.00 per share which raised gross proceeds of $37.3 million. Additionally, the underwriters exercised 779,268 shares of their over-allotment for gross proceeds of $5.5 million or, after deducting underwriters' discount, net proceeds of $5.1 million. Net proceeds from our initial public offering after deducting underwriters discounts and offering expenses was $37.9 million.

At December 31, 2004, we had cash and cash equivalents of $14.3 million compared to $40.6 million at December 31, 2003 and $6.2 million at December 31, 2002. In addition, we had marketable securities balances of $14.3 million, $0.2 million and $45,000 as of December 31, 2004, 2003 and 2002, respectively, available to fund operations. Net cash used in operating activities for the years ended December 31, 2004, 2003 and 2002 was $10.8 million, $6.7 million, and $2.5 million, respectively. For the year ended December 31, 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, an increase in accrued liabilities for clinical trials and staffing, and the receipt of a research and development contract advance under the MediBIC agreement. 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.

Net cash used in investing activities of $15.4 million, $0.2 million and $0.2 million for the years ended December 31, 2004, 2003 and 2002 respectively, was primarily for the acquisition of marketable securities in 2004, the acquisition of property and equipment in 2003 and the purchase of two certificates of deposit, equipment and marketable securities. Net cash used by financing activities was $0.1 million for the year ended December 31, 2004 primarily for deferred costs related to the initial public offering in February 2005. Net cash generated by financing activities was $41.3 million and $8.7 million for the years ended December 31, 2003 and 2002 respectively which was primarily attributable to the sale of redeemable convertible preferred stock.

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 June 15, 2005. We have classified the $5.0 million as a current liability. 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 our cash on hand and marketable securities as of December 31, 2004, plus the net proceeds from our initial public offering completed in February 2005, will be sufficient to fund our projected operating requirements for approximately 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 commercialization effort, working capital and general corporate purposes. However, we will need to raise additional capital or incur indebtedness to continue to fund our operations in the future. We also intend 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. 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.

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 December 31, 2004, we have borrowed the

full amount under this facility, which will be repaid over a 36-month period from the date of borrowing. These borrowings bear interest at an average rate of 5.8% per year at December 31, 2004. At December 31, 2004 the amount due under this facility was $0.7 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 December 31, 2004 we were in compliance with our covenant.

On August 31, 2004, we entered into a noncancelable facilities sublease agreement that expires on February 28, 2010.

As of December 31, 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 sublease	$ 384	$ 1,335	$ 623	$ —	$2,342
Financing line	331	382	—	—	713
Total	$ 715	$ 1,717	$ 623	$ —	$3,055

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 preclinical 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 worldwide 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 (approximately $2.4 million based on the exchange rate at December 31, 2004).

Off-Balance Sheet Liabilities

As of December 31, 2004, 2003 and 2002, 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 Form 10-K, 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 December 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, 2003 and 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, 2003 and 2004. In addition, we determined that the fair value of our common stock increased from $0.16 to $16.39 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 was reasonable to expect that the completion of our initial public offering would add value to the shares as a result of increased liquidity and marketability, the amount of additional value could not 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.

Marketable Securities

We classify all of our marketable securities as available-for-sale. We carry these investments at fair value, based on quoted markets prices, and unrealized gains and losses are included in accumulated other comprehensive income which is reflected as a separate component of stockholders' equity. The amortized cost of securities in this category is adjusted for amortization of premiums and accretions of discounts to maturity. Such amortization is included in interest income. Realized gains and losses are recorded in our statement of operations. If we believe that an other-than-temporary decline exists, it is our policy to record a write-down to reduce the investments to fair value and record the related charge as a reduction of interest income.

During the quarter ended December 31, 2004 we reclassified auction rate securities from cash and cash equivalents to short-term marketable securities. From time to time during the quarters ended June 30, September 30 and December 31, 2004, we invested in auction rate securities. As of June 30, 2004 and September 30, 2004, the Company held $4.7 million and $3.7 million respectively, of auction rate securities, which have been reclassified. The reclassification has no impact on our results of operations. The reclassification will be shown on the balance sheets and statements of cash flows to be filed on Form 10-Q for the periods ending June 30 and September 30, 2005.

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 assets, as based on available objective evidence; it is more likely than not that the deferred tax assets 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 assets would increase net income in the period such determination was made.

Recent Accounting Pronouncements

In December 2004, the FASB issued SFAS No. 123 "*Share-Based Payment. – An Amendment of FASB Statements No. 123 and 95"* ("SFAS No. 123R"). The new pronouncement replaces the existing requirements under SFAS No. 123 and APB No. 25. According to SFAS No. 123R, all forms of share-based payments to employees, including employee stock options and employee stock purchase plans, would be treated as the same as any other form of compensation by recognizing the related cost in the statement of operations. This pronouncement eliminates the ability to account for stock-based compensation transactions using APB No. 25 and generally would require that such transactions be accounted for using a fair-value based method. For public companies, the FASB has determined that SFAS No. 123R is effective for awards and stock options granted, modified or settled in cash in interim or annual periods beginning after June 15, 2005. SFAS No. 123R provides transition alternatives for public companies to restate prior interim periods or prior years. We are in the process of evaluating the impact of this standard on our financial statements.

RISK FACTORS

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. We plan to initiate a Phase 3 trial in several European countries and a Phase 2 trial in the US for this indication by mid-2005; however, we expect regulatory agencies will require addition clinical trials and may require additional preclinical studies to support approval of TH-070 for the treatment of symptomatic BPH.

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. In addition, we are aware that our planned trials for TH-070 for the treatment of symptomatic BPH may be subject to competition for patients by competing trials, which could delay enrollment for our trials.

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. Prior to our initial public offering in February 2005, we financed our operations primarily through private placements of our equity securities. For the year ended December 31, 2004, we had a net loss of $23.6 million and an accumulated deficit of $34.6 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 our clinical trials 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 approvals;
- 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 our initial public offering in February 2005 together with our cash on hand and marketable securities, will be sufficient to fund our projected operating requirements for approximately 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 will need to raise additional capital or incur indebtedness to continue to fund our operations in the future. We also expect to seek funds through arrangements with collaborators or others that may require us to relinquish rights to certain products candidates that we might otherwise seek to develop or commercialize. 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, our founder and President, Dr. George F. Tidmarsh and our Chief Medical Officer, Dr. Alan Colowick. We do not have employment contracts with Drs. Selick, Tidmarsh or Colowick. 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 Drs. Selick, Tidmarsh, or Colowick 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 December 31, 2004, we had 42 employees. 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. Prior to our initial public offering February 2005, we operated as a private company, not subject to many of the requirements applicable to public companies. While we plan to expand our staff, 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, 2006. 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 we conclude that our internal controls over financial reporting are not effective 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, 2006 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 also believe we have received sufficient drug product tested and released by Pharmaceutics International, Incorporated (PPI) for the planned European Phase 3 trial of TH-070 for the treatment of BPH. We have also received enough drug product that has been tested but not yet released by PPI for the planned Phase 2 US trial of TH-070 for the treatment of BPH. We have ordered additional TH-070 API from Jiangsu Hengrui Medicine Company, Ltd. 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. Tarceva, under development by OSI Pharmaceuticals, Genentech and Roche, met its primary endpoint in a Phase 3

combination trial with gemcitabine 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.

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.

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. In addition, since our initial public offering, the average daily trading volume of our common stock was 80,370 shares. The limited trading volume of our stock may contribute to its volatility.

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.

A significant portion of our total outstanding shares are restricted from immediate resale subsequent to our initial public offering in February 2005 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 could adversely affect the price of our common stock. Certain of our existing stockholders and their affiliated entities purchased an aggregate of approximately 1.5 million shares of our common stock in our initial public offering in February 2005. Shares purchased by our affiliates in this offering may only be sold in compliance with the volume limitations of Rule 144. These volume limitations restrict the number of shares that may be sold by an affiliate in any three-month period to the greater of 1% of the number of shares then outstanding, which equals approximately 307,460, or the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Holders of approximately 23,921,574 shares of our common stock entered into lock-up agreements that prevent the sale of such shares for up to 180 days after our initial public offering subject to extension under certain circumstances. After expiration of the lock-ups, these shares will be tradeable subject to Rule 144. Holders of an aggregate of 20,552,815 shares of common stock plus the 1,500,003 additional shares that existing stockholders purchased in our initial public offering have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Due to these factors, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISKS

We do not have any foreign currency or derivative financial instruments. 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 marketable securities.

The primary objective of our investing 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 December 31, 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 December 31, 2004, this facility provides for borrowings up to $1.0 million, which we have fully utilized. At December 31, 2004, approximately $0.7 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 is 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.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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

	Page
Report of Independent Registered Public Accounting Firm	56
Balance Sheets	57
Statements of Operations	58
Statements of Stockholders' Deficit	59
Statements of Cash Flows	60
Notes to Financial Statements	61

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, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, and cumulatively for the period from October 17, 2001 (date of inception) to December 31, 2004, 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
March 30, 2005

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

	December 31, 2004	December 31, 2003
ASSETS		
Current assets:		
Cash and cash equivalents	$ 14,339	$ 40,609
Marketable securities	14,326	209
Prepaid expenses and other current assets	1,604	128
Restricted cash	85	115
Total current assets	30,354	41,061
Property and equipment, net	1,667	199
Restricted cash	192	—
Other assets	—	10
Total assets	$ 32,213	$ 41,270
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 1,550	$ 281
Accrued liabilities	1,506	437
Notes payable, current portion	331	166
Advance on research and development contract (Note 7)	5,000	—
Total current liabilities	8,387	884
Notes payable, less current portion	382	242
Deferred rent	78	—
Total liabilities	8,847	1,126
Commitments and contingencies (Note 7)		
Redeemable convertible preferred stock, $0.001 par value:		
Authorized: 33,886,484 shares		
Issued and outstanding: 33,848,484 shares in 2004 and 2003		
(Liquidation value: $50,000 at December 31, 2004)	49,839	49,839
Stockholders' deficit:		
Common stock, $0.001 par value:		
Authorized: 30,360,070 shares		
Issued and outstanding: 3,690,567 shares in 2004 and 184,709 shares in 2003	4	—
Additional paid-in capital	24,619	2,685
Deferred stock-based compensation	(16,637)	(1,546)
Accumulated other comprehensive income	104	163
Deficit accumulated during the development stage	(34,563)	(10,997)
Total stockholders' deficit	(26,473)	(9,695)
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	$ 32,213	$ 41,270

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)

	Years Ended December 31,			
	2004	2003	2002	Cumulative Period from October 17, 2001 (date of inception) to December 31, 2004
Operating expenses:				
Research and development	$ 16,327	$ 6,252	$ 2,179	$ 24,793
General and administrative	7,649	2,057	306	10,213
Total operating expenses	23,976	8,309	2,485	35,006
Loss from operations	(23,976)	(8,309)	(2,485)	(35,006)
Interest income	443	65	27	535
Interest expense	(33)	(59)	—	(92)
Net loss	(23,566)	(8,303)	(2,458)	(34,563)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	(40,862)	—	(40,862)
Net loss attributable to common stockholders	$ (23,566)	$ (49,165)	$ (2,458)	$ (75,425)
Net loss per common share:				
Basic and diluted	$ (20.25)	$ (501.68)	$ (34.62)	
Weighted average number of shares used in per common share calculations:				
Basic and diluted	1,164	98	71	

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 DECEMBER 31, 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	3,518,304	4	874	—	—	—	878
Deferred stock-based compensation, net of cancellations	—	—	20,385	(20,385)	—	—	—
Amortization of deferred stock-based compensation	—	—	—	5,294	—	—	5,294
Non-employee stock-based compensation	—	—	681	—	—	—	681
Repurchase of unvested common stock	(12,446)	—	(6)	—	—	—	(6)
Components of other comprehensive income (loss):							
Change in unrealized gain (loss) on marketable securities	—	—	—	—	(59)	—	(59)
Net loss	—	—	—	—	—	(23,566)	(23,566)
Comprehensive loss							(23,625)
Balances, December 31, 2004	3,690,567	$ 4	$ 24,619	$ (16,637)	$ 104	$ (34,563)	$ (26,473)

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

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

	Years Ended December 31,			Cumulative Period from October 17, 2001 (date of inception) to December 31, 2004
	2004	2003	2002	
Cash flows from operating activities:				
Net loss	$(23,566)	$ (8,303)	$(2,458)	$ (34,563)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation	143	90	11	244
Stock-based compensation expense	5,975	1,066	22	7,063
Amortization of debt issuance costs	10	34	—	44
Loss on disposal of property and equipment	—	—	5	5
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(189)	152	(272)	(317)
Accounts payable	699	(32)	262	980
Accrued liabilities	1,050	334	(39)	1,487
Advance on research and development contract	5,000	—	—	5,000
Deferred rent	78	—	—	78
Net cash used in operating activities	(10,800)	(6,659)	(2,469)	(19,979)
Cash flows from investing activities:				
Acquisition of property and equipment	(1,022)	(218)	(87)	(1,327)
Acquisition of marketable securities	(38,199)	—	(46)	(32,495)
Proceeds from sale of marketable securities	24,023	—	—	18,273
Restricted cash	(162)	—	(115)	(277)
Net cash used in investing activities	(15,360)	(218)	(248)	(15,826)
Cash flows from financing activities:				
Proceeds from redeemable convertible preferred stock, net	—	40,862	8,741	49,839
Proceeds from issuance of common stock, net	872	1	4	879
Deferred financing costs	(1,287)	—	—	(1,287)
Proceeds from issuance of notes payable	490	510	—	1,000
Repayment of notes payable	(185)	(102)	—	(287)
Net cash provided by (used in) financing activities	(110)	41,271	8,745	50,144
Net increase (decrease) in cash and cash equivalents	(26,270)	34,394	6,028	14,339
Cash and cash equivalents, beginning of period	40,609	6,215	187	—
Cash and cash equivalents, end of period	$ 14,339	$40,609	$ 6,215	$ 14,339
Supplemental disclosures:				
Cash paid for interest	$ 33	$ 14	$ —	$ 47
Non-cash investing and financing activities:				
Accrued cost of acquisition of property and equipment	$ 589	$ —	$ —	$ 589
Deferred stock-based compensation	$ 20,385	$ 2,332	$ 25	$ 22,742
Fair value of redeemable convertible preferred stock warrant	$ —	$ 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.

All common share and per share amounts and the conversion ratios of the redeemable convertible preferred stock contained in the accompanying financial statement have been retroactively adjusted to reflect the stock split described in Note 12.

NOTE 2—SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES:

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America.

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.

Marketable securities include auction rate securities. These securities are structured as short-term, highly liquid investments that can be readily converted into cash every 30, 60 or 90 days. However, since the stated or contractual maturity of these securities is greater than 90 days, these securities are classified as marketable securities.

Fair value of financial instruments

The 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, 2004 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 has three drug candidates in development, none of which 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.

Deferred financing costs

Deferred financing costs include legal, accounting, printing, registration, and other costs associated with the Company's initial public offering. These costs are classified as a current asset and will be offset against the proceeds of our initial public offering.

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. Leasehold improvements are amortized using the straight-line method over the estimated useful life of the improvement, or the lease term, if shorter. 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," ("SFAS No. 144") 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, 2004, the Company has not incurred any such impairment losses.

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.

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.

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.

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):

	Years Ended December 31,		
	2004	2003	2002
Numerator:			
Net loss	$(23,566)	$ (8,303)	$(2,458)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	(40,862)	—
Net loss attributable to common stockholders	$(23,566)	$(49,165)	$(2,458)
Denominator:			
Weighted-average number of common shares outstanding	2,335	183	174
Less: Weighted-average shares subject to repurchase	(1,171)	(85)	(103)
Weighted-average number of common shares outstanding used in computing basic and diluted net loss per common share	1,164	98	71

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,		
	2004	2003	2002
Redeemable convertible preferred stock	33,848	33,848	9,000
Options to purchase common stock	447	1,791	1,078
Common stock subject to repurchase	2,069	76	95
Warrants to purchase redeemable convertible preferred stock	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 ("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):

	Years Ended December 31,		
	2004	2003	2002
Net loss attributable to common stockholders, as reported	$(23,566)	$(49,165)	$(2,458)
Add: Employee stock-based compensation included in reported net loss	5,294	810	1
Deduct: Employee total stock-based compensation determined under fair value method	(3,601)	(815)	(13)
Pro forma net loss attributable to common stockholders	$(21,873)	$(49,170)	$(2,470)
Net loss attributable to common stockholders per common share, basic and diluted:			
As reported	$ (20.25)	$(501.68)	$(34.62)
Pro forma	$ (18.79)	$(501.73)	$(34.79)

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,		
	2004	2003	2002
Weighted average risk-free interest rate	2.77%	1.98%	2.98%
Expected life (in years)	4	4	4
Dividend yield	—	—	—

The grant date weighted average fair value per share of options granted during the years ended December 31, 2004, 2003 and 2002 was $9.01, $3.47, and $0.05, respectively.

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 December 2004, the FASB issued SFAS No. 123 *"Share-Based Payment.—An Amendment of FASB Statements No. 123 and 95"* ("SFAS No. 123R"). The new pronouncement replaces the existing requirements under SFAS No. 123 and APB No. 25. According to SFAS No. 123R, all forms of share-based payments to employees, including employee stock options and employee stock purchase plans, would be treated as the same as any other form of compensation by recognizing the related cost in the statement of operations. This pronouncement eliminates the ability to account for stock-based compensation transactions using APB No. 25 and generally would require that such transactions be accounted for using a fair-value based method. For public companies, the FASB has determined that SFAS No. 123R is effective for awards and stock options granted, modified or settled in cash in interim or annual periods beginning after June 15, 2005. SFAS No. 123R provides transition alternatives for public companies to restate prior interim periods or prior years. We are in the process of evaluating the impact of this standard on our financial statements.

NOTE 3—MARKETABLE SECURITIES:

As of December 31, 2004 (in thousands):	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
Common stock in a public company	$ 46	$ 121	$ —	$ 167
Corporate bonds	3,701	—	(11)	3,690
Government securities	4,285	—	(5)	4,280
Commercial paper	3,990	—	(1)	3,989
Auction rate securities	2,200	—	—	2,200
Total	$14,222	$ 121	$ (17)	$14,326

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

All marketable securities mature within one year. Realized gains or losses from the sales of marketable securities for the years ended December 31, 2004, 2003 and 2002 were not material.

NOTE 4—PROPERTY AND EQUIPMENT:

Property and equipment comprise the following (in thousands):

	December 31,	
	2004	2003
Laboratory equipment	$ 437	$ 270
Computer and office equipment	73	30
Leasehold improvements	1,401	—
	1,911	300
Less: Accumulated depreciation	(244)	(101)
	$1,667	$ 199

NOTE 5—ACCRUED LIABILITIES:

Accrued liabilities comprise the following (in thousands):

	December 31,	
	2004	2003
Professional services	$ 395	$ 115
Payroll and employee related expenses	449	77
Clinical expenses	426	217
Other accrued expenses	236	28
	$ 1,506	$ 437

NOTE 6—NOTES PAYABLE:

On March 27, 2003, the Company entered into a line of credit agreement with a financial institution under which the Company could borrow up to $1,000,000 for working capital requirements and 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, 2004, the Company had borrowed $300,000 under its working capital line of credit and $700,000 under the equipment line of credit, for borrowings of $1,000,000 at an average interest rate of 5.8% per annum and has repaid $287,000. Borrowings under the equipment line of credit are collateralized by the related equipment. In connection with the agreement, the Company issued to the financial institution a warrant to purchase 38,000 shares of Series A redeemable convertible preferred stock (Note 8).

At December 31, 2004, future principal payments under the notes payable are as follows (in thousands):

Year Ending December 31,	
2005	$331
2006	230
2007	152
Total	$713

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, 2004, 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 expired on December 31, 2004. 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 (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 Company recognizes the rent expense using the straight line method. The future rental payments required by the Company under the noncancelable operating sublease as of December 31, 2004 are as follows (in thousands):

Years Ended December 31,	
2005	$ 384
2006	400
2007	417
2008	518
2009 and thereafter	623
Future minimum rental payments	$ 2,342

Rent expense for the years ended December 31, 2004, 2003, 2002 and, cumulatively, for the period from October 17, 2001 (date of inception) to December 31, 2004 was $726,000, $447,000, $ 112,000 and $1,311,000, respectively.

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, 2004.

In August 2003, the Company entered into an exclusive worldwide license and development agreement with a corporation for certain patent rights and technology associated with glufosfamide and its drug candidates in development. Under the terms of the agreement, the Company made an initial upfront payment of $100,000 and in December 2003, another 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, 2004.

In June 2004, the Company entered into an agreement with a corporation for rights to use regulatory documents and preclinical 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 a one-time payment of approximately $374,000, in 2004. The Company is also obligated to pay 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 (approximately $2.4 million based on the exchange rate at December 31, 2004).

In November 2004, the Company entered into a Development Agreement with a corporate partner. Under this agreement, the Company 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. The Company will be required to refund these payments and the agreement will terminate if the Company and its partner cannot agree to the development plan by June 15, 2005, or a later date agreed by the parties. Therefore, the $5.0 million received has been classified as an advance on research and development contract on the accompanying balance sheet. The Company is responsible for all development activities and 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 ranging from $5.25 to $15 million, depending on the stage of development. The Chief Operating Officer who is also a director of a subsidiary of the partner, is the wife of the Company's Chief Executive Officer.

Indemnification

The Company enters into indemnification provisions under its agreements with other companies in the ordinary course of business, including business partners, contractors and parties performing its clinical trials. Pursuant to these arrangements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified parties for losses suffered or incurred by the indemnified party as a result of the Company's

activities. The terms of these indemnification agreements are generally perpetual. The maximum potential amount of future payments the Company could be required to make under these agreements is not determinable. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. As a result, the Company believes the estimated fair value of these agreements is minimal. The 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.

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, 2003 and 2004, 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	

As of December 31, 2004, 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 December 31, 2004 no dividends had been declared on any class of the Company's capital stock.

Liquidation

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

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

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

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

Redemption

The merger or consolidation of the Company into another entity or any transactions in which more than 50% of the voting power of the Company is disposed of or the sale, transfer or disposition of substantially all of the 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 non-assessable 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, 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' discount and other offering costs, and with a pre-money valuation not less than $200,000,000.

All of the shares of redeemable convertible preferred stock were converted into 20,552,815 shares of common stock upon completion of the Company's initial public offering (Note 12).

Voting rights

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

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

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

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

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, 2004.

On October 24, 2001, shares of restricted stock were issued to the Company's founder and member of the Board of Directors under a restricted stock purchase agreement. On January 29, 2002, shares of restricted common stock were issued to a member of the Board of Directors under a restricted stock purchase agreement. Generally, the shares vest over a four-year period. The unvested shares of common stock are subject to repurchase by the Company in the event of termination of the employment or consulting relationship. Included in common stock as of December 31, 2004, 2003 and 2002 are 55,168, 75,970 and 95,367 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, 2004, 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 December 31, 2004 are 2,013,977 shares subject to repurchase relating to options exercised prior to vesting at the lesser of fair market value or the exercise price.

Activity under the 2001 Plan is set forth below:

		Outstanding Options		
	Shares Available for Grant	Number of Shares	Exercise Price	Weighted Average 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	(2,222,333)	2,222,333	0.26–0.53	0.36
Options exercised	—	(3,518,304)	0.16–0.53	0.25
Options canceled	47,573	(47,573)	0.16–0.53	0.28
Balances, December 31, 2004	274,629	447,337	$ 0.16–0.53	$ 0.45

At December 31, 2004, 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	74,595	7.78	49,997	$ 0.16
$0.26	26,946	9.19	4,743	0.26
$0.53	345,796	9.64	8,770	0.53
	447,337		63,510	$ 0.21

At December 31, 2003, the Company had 922,369 stock options vested at a weighted average exercise price of $0.16 per share.

Deferred stock-based compensation

During the years ended December 31, 2004, 2003, and 2002, 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, 2004, 2003 and 2002, the Company has recorded deferred stock-based compensation related to these options of approximately $14,376,000, $2,332,000 and $25,000, net of cancellations, respectively.

In May 2004, the Company granted 386,778 options to employees to purchase shares of common stock at $0.53 per share. These options contained a call feature that allowed the Company to cancel the options by January 31, 2005 if the Company did not complete an initial public offering by December 31, 2004. If the Company had elected to exercise this call feature, the outstanding options would have been cancelled and any shares purchased pursuant to exercise of the options would be immediately repurchasable by the Company at the original purchase price. On December 14, 2004 the Company's Board of Directors eliminated the call feature. Prior to the elimination of the call feature the Company applied variable accounting to these options, resulting in deferred stock-based compensation of $6,009,000 and stock compensation expense of $2,359,000 during the year ended December 31, 2004. Stock compensation expense was 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 December 31, 2004, 257,444 of these options had been early exercised and not vested.

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

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
December 31, 2004	160	0.53	16.39	15.86

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,		
	2004	2003	2002
Research and development	$2,279	$ 57	$—
General and administrative	3,015	753	1
	$5,294	$810	$ 1

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, 2004, 2003 and 2002, the Company issued options to non-employees. The options generally vest ratably over the time period the Company expects to receive services from the non-employee. 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 valuation model as prescribed by SFAS No. 123 using the following assumptions:

	Years Ended December 31,		
	2004	2003	2002
Risk-free interest rate	4.38%	4.26%	4.76%
Expected life (in years)	10	10	10
Dividend yield	—	—	—
Expected volatility	70%	70%	70%

The stock-based compensation expense will fluctuate as the 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 $681,000, $256,000 and $21,000, for the years ended December 31, 2004, 2003 and 2002, respectively. Stock-based compensation expenses related to options granted to non-employees were entirely expensed to research and development.

NOTE 10—INCOME TAXES:

A reconciliation of income taxes at the statutory federal income tax rate to net income taxes included in the accompanying statements of operations is as follows (in thousands):

	2004	2003	2002
U.S. federal taxes (benefit) at statutory rate	$(8,013)	$(2,823)	$(836)
State federal income tax benefit	(1,374)	—	—
Unutilized (utilized) net operating losses	6,075	2,539	833
Stock-based compensation	1,919	276	—
Research and development credits	(554)	—	—
Tax assets not benefited	1,947	8	3
Total	$ 0	$ 0	$ 0

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

	December 31,		
	2004	2003	2002
Capitalized start-up costs	$ 1,014	$ 605	$ 126
Net operating loss carryforwards	9,482	3,407	947
Research and development credits	874	385	88
Other (stock-based compensation, accruals, reserves, depreciation)	852	49	4
Total deferred tax assets	12,222	4,446	1,165
Less: Valuation allowance	(12,222)	(4,446)	(1,165)
	$ —	$ —	$ —

At December 31, 2004, the Company had federal and state net operating loss carryforwards of approximately $23,803,000 and $23,802,000 available to offset future regular taxable income. The Company's federal and state net operating loss carryforwards will begin to expire in 2022 and 2014, 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. The annual limitation may result in the expiration of the net operating loss before utilization.

At December 31, 2004, the Company had research credit carryforwards of approximately $509,000 and $553,000 for federal and state income tax purposes, respectively. If not utilized, the federal carryforwards will expire in various amounts beginning in 2022. 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, 2004, the Company did not make any contributions to the 401(k) Plan.

NOTE 12—SUBSEQUENT EVENTS:

Initial Public Offering

On February 4, 2005, the Company sold 5,333,333 shares of common stock in an initial public offering for aggregate gross proceeds of $37,333,000. After deducting the underwriters commission and offering expenses, the Company received net proceeds of $32,800,000. On March 4, 2005 the Company received an aggregate of $5,455,000 from the exercise of the underwriters over allotment. After deducting the underwriter's commission, the Company received net proceeds of $5,073,000. Upon completion of the initial public offering all redeemable convertible preferred stock converted to common stock.

2004 Equity Incentive Plan

On April 7, 2004, the Board of Directors adopted the 2004 Equity Incentive Plan (the "2004 Plan"), and received stockholder approval on January 10, 2005. The 2004 Plan became 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, 2006, 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

Effective with the initial public offering, the Board of Directors approved the 2004 Employee Stock Purchase Plan (the "Purchase Plan"). 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.

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. The stock split was affected on January 26, 2005. All common share and per share amounts and the conversion ratios of the redeemable convertible preferred stock contained in the accompanying financial statements were retroactively adjusted to reflect the stock split.

Changes to the Articles of Incorporation

On April 7, 2004 the Company's Board of Directors adopted an Amended and Restated Certificate of Incorporation ("Amended Certificate"), and received stock holder approval on January 10, 2005. The Amended Certificate became effective upon completion of the Company's initial public offering and increases the number of shares, to 150,000,000 shares of common stock and 2,000,000 shares of preferred stock, both with par values of $0.001 per share.

NOTE 13—QUARTERLY FINANCIAL DATA (UNAUDITED)

The following table presents certain unaudited quarterly financial information for the eight quarters ended December 31, 2004. In management's opinion, this information has been prepared on the same basis as the audited financial statements and includes all adjustments necessary to present fairly the unaudited quarterly results of operations ended December 31, 2004, and 2003.

2004	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share data)				
Net loss attributable to common stockholders	$ (2,793)	$ (6,262)	$ (6,648)	$ (7,863)
Basic and diluted net loss per share attributable to common stockholders	$ (23.87)	$ (5.83)	$ (4.80)	$ (5.05)
Shares used in computation of basic and diluted net loss per share	117	1,075	1,385	1,556
2003				
(in thousands, except per share data)				
Net loss attributable to common stockholders (1)	$ (2,079)	$ (2,447)	$ (1,940)	$ (42,699)
Basic and diluted net loss per share attributable to common stockholders	$ (23.90)	$ (25.50)	$ (18.84)	$ (391.73)
Shares used in computation of basic and diluted net loss per share	87	96	103	109

(1) For the year ended December 31, 2003, we recorded a non-cash dividend of $40.9 million in the 4th quarter. This related to the issuance of convertible preferred shares and the beneficial conversion feature of preferred stock.

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

None

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of disclosure controls and procedures

As required by Exchange Act Rule 13a-15(b), as of the close of our fiscal year ended December 31, 2004, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rule 13a-15(e). Based upon that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures are effective at the reasonable assurance level.

We intend to review and evaluate the design and effectiveness of our disclosure controls and procedures on an ongoing basis and to correct any material deficiencies that we may discover. Our goal is to ensure that our senior management has timely access to material information that could affect our business. While we believe the present design of our disclosure controls and procedures is effective to achieve our goal, future events affecting our business may cause us to modify our disclosure controls and procedures. The effectiveness of controls cannot be absolute because the cost to design and implement a control to identify errors or mitigate the risk of errors occurring should not outweigh the potential loss caused by errors that would likely be detected by the control. Moreover, we believe that disclosure controls and procedures cannot be guaranteed to be 100% effective all of the time. Accordingly, a control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met.

Changes in internal controls

There have been no significant changes in our internal controls or in other factors that could significantly affect these controls subsequent to the date of the evaluation referred to above, nor were there any material weaknesses in our internal controls. Accordingly, no corrective actions were required or undertaken.

ITEM 9B. OTHER INFORMATION

On March 3, 2005, our Board of Directors approved the recommendation of the Compensation Committee of our Board of Directors to award discretionary bonuses to each of Dr. Harold E. Selick, our Chief Executive Officer and a member of our Board of Directors, Dr. George Tidmarsh, our founder, President and a member of our Board of Directors, and Janet I. Swearson, our Chief Financial Officer and Vice President Finance and Operations, in the amounts of $100,000, $75,000, and $50,000, respectively, based on performance during 2004. On such date, the Board of Directors also approved the recommendation of the Compensation Committee to increase the annual base salary for each of Dr. Selick, Dr. Tidmarsh, and Ms. Swearson bringing their respective base salaries for 2005 to $400,000 per year, $300,000 per year and $245,000 per year. Each will also be eligible for discretionary performance bonuses for 2005 of up to thirty percent of his or her respective base salary as recommend by the Compensation Committee and approved by the Board of Directors.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information required by this Item will be contained in the Proxy Statement under the caption “Proposal 1 – Election of Directors” to be filed within 120 days after December 31, 2004 and is hereby incorporated by reference.

ITEM 11. EXECUTIVE COMPENSATION

Information required by this item will be contained in the Proxy Statement under the caption “Executive Compensation” to be filed within 120 days after December 31, 2004 and is hereby incorporated by reference.

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

Information required by this item will be contained in the Proxy Statement under the caption “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” to be filed within 120 days after December 31, 2004 and is hereby incorporated by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Information required by this item will be contained in the Proxy Statement under the caption “Certain Transactions” to be filed within 120 days after December 31, 2004 and is hereby incorporated by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information required by this item will be contained in the Proxy Statement under the caption “Auditor’s Fees” to be filed within 120 days after December 31, 2004 and is hereby incorporated by reference.

PART I V

ITEM 15. EXHIBITS AND FI NANCIAL STATEMENT SCHEDULES

The following documents are being filed as part of this report:

(1) The following financial statements of the Company and the report of PricewaterhouseCoopers LLP are included in Part II, Item 8:

Report of Independent Registered Public Accounting Firm
Balance Sheets
Statements of Operations
Statements of Stockholders' Deficit
Statements of Cash Flows
Notes to the Financial Statements

(2) All financial statement supporting schedules are omitted because the information is inapplicable or presented in the Notes to Financial Statements.

EXHIBIT NUMBER	DESCRIPTION
3.1(1)	Amended and Restated Certificate of Incorporation of the Registrant
3.2(2)	Amended and Restated Bylaws of the Registration
4.1(3)	Specimen Certificate evidencing shares of common stock
4.2(3)	Warrant to purchase stock, issued to Silicon Valley Bank on March 27, 2003
4.3(3)	Amended and Restated Investor Rights Agreement dated as of November 17, 2003 among the Registrant and the parties listed therein
4.4(3)	Form of Amendment No. 1 to Amended and Restated Investor Rights Agreement among the Registrant and certain parties to the Amended and Restated Investor Rights Agreement
10.1(3)	2001 Equity Incentive Plan
10.2(3)	2004 Equity Incentive Plan
10.3(3)	2004 Employee Stock Purchase Plan
10.4(3)	Sub-Lease Agreement by and between Thervance, Inc., a Delaware corporation, and the Registrant dated as of December 5, 2002
10.5(3)	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†(3)	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†(3)	Exclusive License Agreement by and between the Registrant, Dr. Theodore Lampidis and Dr. Waldemar Priebe, dated as of November 11, 2002
10.8(3)	Loan and Security Agreement by and between the Registrant and Silicon Valley Bank, dated March 27, 2003
10.9(3)	Form of Indemnification Agreement by and between the Registrant and its officers and directors
10.10†(3)	Agreement by and between the Registrant and Aziende Chimiche Riunite Angelini Francesco - Acraf S.p.a. dated as of June 24, 2004
10.11(3)	Sublease by and between the Registrant and ArQule, Inc. dated as of August 31, 2004

EXHIBIT NUMBER	DESCRIPTION
10.12(3)	Offer Letter by and between the Registrant and William A. Halter dated as of September 3, 2004
10.13(3)	Offer Letter by and between the Registrant and George G.C. Parker dated as of September 3, 2004
10.14†(3)	Development Agreement by and between the Registrant and MediBIC Co. Ltd., dated as of November 30, 2004
10.15(3)	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(3)	Change of Control Severance Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004
10.17(3)	Stock Vesting Agreement by and between the Registrant and George F. Tidmarsh dated as of December 23, 2004
10.18(3)	Letter Agreement amending Development Agreement by and between the Registrant and MediBIC Co. Ltd.
31.1	Certification Pursuant to Rule 15d-14 of the Securities and Exchange Act of 1934, as amended, as Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification Pursuant to Rule 15d-14 of the Securities and Exchange Act of 1934, as amended, as Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

(1) Filed as Exhibit 3.2 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004, and incorporated herein by reference.

(2) Filed as Exhibit 3.4 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004, and incorporated herein by reference.

(3) Filed as the like number to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004, and incorporated herein by reference.

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

Table of Contents

SIGNATURES

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

THRESHOLD PHARMACEUTICALS, INC.

March 31, 2005

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

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

Signature	Title	Date
/S/ HAROLD E. SELICK, PH.D. **Harold E. Selick, Ph.D.**	Chief Executive Officer (principal executive officer)	March 31, 2005
/S/ JANET I. SWEARSON **Janet I. Swearson**	Chief Financial Officer (principal financial and accounting officer)	March 31, 2005
/S/ GEORGE F. TIDMARSH, M.D., PH.D. **George F. Tidmarsh, M.D., PH.D.**	Founder, Director and President	March 31, 2005
/S/ MICHAEL F. POWELL, PH.D. **Michael F. Powell, Ph.D.**	Director	March 31, 2005
/S/ RALPH E. CHRISTOFFERSEN, PH.D. **Ralph E. Christoffersen, Ph.D.**	Director	March 31, 2005
/S/ PATRICK G. ENRIGHT **Patrick G. Enright**	Director	March 31, 2005
/S/ WILFRED E. JAEGER, M.D. **Wilfred E. Jaeger, M.D.**	Director	March 31, 2005
/S/ WILLIAM A. HALTER **William A. Halter**	Director	March 31, 2005
/S/ GEORGE G. C. PARKER, PH.D. **George G. C. Parker, Ph.D.**	Director	March 31, 2005

Exhibit 31.1

Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Harold E. Selick, certify that:

1. I have reviewed this Form 10-K of Threshold Pharmaceuticals, Inc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) [Paragraph omitted pursuant to SEC Release 33-8238];
   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent function):
   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2005

/s/ HAROLD E. SELICK, PH.D.
Harold E. Selick, Ph.D.
Chief Executive Officer

Exhibit 31.2

Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Janet I. Swearson, certify that:

1. I have reviewed this Form 10-K of Threshold Pharmaceuticals, Inc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) [Paragraph omitted pursuant to SEC Release 33-8238];

   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent function):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2005

/s/ JANET I. SWEARSON
Janet I. Swearson
Chief Financial Officer

Exhibit 32.1

Certifications of the Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Threshold Pharmaceuticals, Inc

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Threshold Pharmaceuticals, Inc (the "Company") on Form 10-K for the year ended December 31, 2004, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Harold E. Selick, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2005

/s/ Harold E. Selick, Ph.D.
Harold E. Selick, Ph.D.
Chief Executive Officer

Exhibit 32.2

Certifications of the Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Threshold Pharmaceuticals, Inc

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Threshold Pharmaceuticals, Inc (the "Company") on Form 10-K for the year ended December 31, 2004, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Janet I. Swearson, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2005

/s/ Janet I. Swearson

Janet I. Swearson
Chief Financial Officer