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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, 2005

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 is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark whether the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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 registrant is a large accelerated filer, an accelerated filer or a non accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act (Check One):

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒

Indicate by check mark whether the registrant is a shell company (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 upon the closing price of the Common Stock on the Nasdaq National Market on June 30, 2005 was $67,737,710. Shares of Common Stock held by each executive officer and director and by each person or group who owns 5% or more of the outstanding Common Stock at June 30, 2005 have been excluded. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

On March 17, 2006 there were 37,284,469 shares of the registrant's common stock outstanding.

Documents incorporated by reference: Portions of the Proxy Statement for Registrant's Annual Meeting of Stockholders to be held May 25, 2006, or the Proxy Statement, are incorporated herein by reference into Part III.

Threshold Pharmaceuticals, Inc.
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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 within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We may, in some cases, use words such as "project," "believe," "anticipate," "plan," "expect," "estimate," "intend," "should," "would," "could," "potentially," "will," or "may," or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements may include statements about:

- our ability to commence, and the timing of, clinical trials for our TH-070, glufosfamide and 2DG development programs;
- the completion and success of any clinical trials that we commence;
- the timing of results of our clinical trials;
- our receipt of regulatory approvals;
- our ability to establish and maintain intellectual property rights in our product candidates;
- whether any product candidates that we are able to commercialize are safer or more effective than other marketed products, treatments or therapies;
- our research and development activities, including development of new product candidates, and projected expenditures;
- our ability to successfully complete preclinical and clinical testing for new product candidates that we may develop or license;
- our ability to have manufactured sufficient supplies of active pharmaceutical ingredient, or 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 annual report on Form 10-K under the caption "Risk Factors." You should read these factors and the other cautionary statements made in this annual report on Form 10-K as being applicable to all related forward-looking statements wherever they appear in this annual report on 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. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. Unless the context requires otherwise, in this annual report on Form 10-K the terms "Threshold," "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 annual report on Form 10-K are the property of their respective owners.

ITEM 1. BUSINESS

Overview

We are a biotechnology company focused on the discovery, development and commercialization of drugs based on Metabolic Targeting, an approach that targets fundamental differences in metabolism between normal

and certain diseased cells. We are building a pipeline of drugs that are designed to selectively target tumor cells and abnormally proliferating cells so that the drugs are more efficacious and less toxic to healthy tissues than conventional drugs, thereby providing improvements over current therapies.

Our initial clinical programs focus on product candidates for the treatment of benign prostatic hyperplasia, or BPH, a disease characterized by overgrowth of the prostate, and of cancer. We have three product candidates for these programs, for which we have exclusive worldwide marketing rights:

- TH-070 is our lead product candidate for the treatment of symptomatic BPH. We completed enrollment in March 2006 in a Phase 2 trial that was initiated in the United States in June 2005 and expect to complete enrollment in April 2006 in a Phase 3 trial that was initiated in Europe in August 2005. Both of these trials are multi-centered, randomized, blinded and placebo controlled trials. We previously completed a single center Phase 2 clinical trial in Italy.
- Glufosfamide is our lead product candidate for cancer. We initiated a pivotal Phase 3 clinical trial of glufosfamide for the second-line treatment of pancreatic cancer in September 2004. We have received a special protocol assessment from the United States Food and Drug Administration, or FDA, for this trial. Glufosfamide for the second-line treatment of pancreatic cancer has also received FDA Fast Track designation. Also in January 2006, we initiated the Phase 2 stage of a study of glufosfamide plus gemcitabine for the first-line treatment of advanced pancreatic cancer, after completing a Phase 1 dose-escalation study in patients with advanced solid tumors and pancreatic cancer.
- 2-deoxyglucose, or 2DG, our product candidate for the treatment of solid tumors, is being evaluated in a Phase 1 clinical trial alone and as a combination therapy. 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. We are investigating additional compounds for activity against BPH.

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, which include decreased libido, impotence, abnormal ejaculation, rhinitis and cardiovascular effects such as dizziness, fainting and lightheadedness. For the treatment of cancer, we believe that our product candidates, based on Metabolic Targeting, can be applied to the treatment of many solid tumors and will 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. 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. BPH, which often leads to debilitating urinary problems, affects 50% of men in their fifties and up to 90% of men over 80, and current treatments have significant deficiencies. Approximately 18 million men in the United States, 28 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 treatment for BPH that is more effective and has fewer side effects than existing therapies. Cancer is the second leading cause of death in the United States after cardiovascular disease. Many cancers, such as pancreatic, lung and liver cancer, have few effective treatments and very low survival rates.

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, as well as a subset of cells in the prostate, rely predominantly or exclusively on glycolysis for their energy needs. 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 BPH

We are using Metabolic Targeting to develop a new class of drugs for BPH that may offer a significant improvement over current treatments. BPH is an overgrowth of prostate cells that restricts urine flow and causes a number of debilitating symptoms. 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 sufficient energy from the citric acid cycle. This process is mediated by the accumulation of high levels of zinc, which blocks citrate metabolism and inhibits 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 and other processes that are essential for prostate cell viability. Preclinical studies and our Phase 2 data suggest that our product candidate TH-070 may inhibit glycolysis and kill prostate cells disproportionately because normal cells can rely on the citric acid cycle for energy production.

Metabolic Targeting For Cancer

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

We are focused on developing new cancer therapies by targeting the intake and metabolism of glucose by cells. In one application of Metabolic Targeting, we use a cancer-killing drug linked to glucose to take advantage of increased glucose intake by cancer cells, thereby delivering the drug more 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 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 intake by these cells by linking a cancer-killing drug to glucose, which enters these cells at relatively higher levels compared to most normal cells. Our product candidate 2-DG targets glucose metabolism directly and provides 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. 2-DG, our product candidate that reduces cellular energy production, inhibits 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. Interference with cellular energy production can disrupt this multidrug resistance, resulting in increased chemotherapy drug accumulation within the cell. We believe our 2DG product candidate will therefore increase the effectiveness of chemotherapy drugs by interfering with cellular energy production.

In addition to treating rapidly dividing cancer cells, we believe that compounds based on Metabolic Targeting provide 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 that, 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 either their increased glucose transport or glucose metabolism.

Our Product Development Programs

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

Product Candidate	Indication	Development Status	Expected Milestones
TH-070	BPH	• US Phase 2 in progress	• Results around the beginning of 4th quarter 2006
			• Results around the beginning of 4th quarter 2006
		• EU Phase 3 in progress	• Commence in 2006
		• 3 supportive studies	
Glufosfamide	Pancreatic cancer	• Phase 3 in progress for second-line single-agent	• Results end of 2006
		• Phase 2 in progress for first-line in combination with gemcitabine	• Early response data end of 2006 and 6-month survival data in 2007
		• Phase 2	
	Additional indication(s)		• Commence in 2006
2DG	Various solid tumors	• Phase 1 in progress	• Results end of 2006

TH-070

BPH Market Opportunity

In 2004, it was estimated that worldwide sales of drugs used to treat BPH were at least $2.8 billion. The American Urological Association, or AUA, estimates that more than 50% of men in their fifties and up to 90% of men over 80 have some symptoms of BPH. Approximately 18 million men in the United States, 28 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 treatment for BPH that is more effective and has fewer side effects. Less than 25% of patients that are symptomatic for BPH are diagnosed, and approximately two-thirds of those diagnosed

receive medical therapy. In the United States alone, it is estimated that two million men are treated with drugs for BPH. These numbers are expected to increase in the future due to increased awareness and the aging population.

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

Current Therapies for BPH

Current therapies for BPH either address its symptoms but not the underlying condition, or block growth of new prostate cells and reduce prostate size with only moderate relief of symptoms. There are two classes of drugs to treat BPH. The first, alpha adrenergic receptor blockers, such as Flomax, are believed to work by relaxing the smooth muscle in the urethra and bladder without addressing the underlying condition of the enlarged 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. Drugs in the second category, 5-alpha reductase inhibitors, such as Proscar and Avodart, work by blocking production of the hormones that stimulate the growth of new prostate cells thereby stopping and eventually reversing enlargement of the prostate. 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. Drugs in both classes can have significant side effects, including decreased libido, impotence, abnormal ejaculation, rhinitis and cardiovascular effects such as dizziness, fainting and lightheadedness. 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. We believe our product candidate TH-070 provides rapid relief of the symptoms of BPH as well as treats the underlying disease by reducing prostate size.

Potential Advantages of TH-070

TH-070, our lead product candidate for the treatment of symptomatic BPH, works by a novel mechanism. It 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 targeting the metabolism of glucose and other processes that are essential for prostate cell viability, TH-070 kills prostate cells, reducing the size of the prostate, and therefore may provide an effective treatment for symptomatic BPH. We expect TH-070 may reduce the size of the prostate more rapidly than current medical treatments and may rapidly improve symptoms, without the attendant side effects of other drugs, which include decreased libido, impotence, abnormal ejaculation, rhinitis and cardiovascular effects such as dizziness, fainting and lightheadedness. We initially selected TH-070, reported to be a glycolysis inhibitor, to treat BPH based on our understanding that prostate cells rely predominantly on glycolysis for energy production as well as published animal and human clinical data demonstrating tolerability of this drug.

Prior Clinical Trials

We have completed a Phase 2 clinical trial 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. Based on promising interim data from the low-dose group of patients in this study, we elected not to enroll the high-dose group.

In this Phase 2 trial, patients were evaluated at several timepoints for safety and specific efficacy parameters, including prostate size, maximum urine flow rate, prostate specific antigen levels, or PSA, residual volume of urine, 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 for our trial was a comparison of prostate size, as measured by volume, between baseline and day 28 of treatment.

In the trial we observed improvements in all variables that were 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 an observed result is random. The smaller the p-value, the lower the likelihood that the observed result was random. Generally, a p-value of 0.05 or less is considered statistically significant. Additionally, after six months of follow-up after the last dose of active drug, all efficacy endpoints remained improved and statistically different than baseline, other than prostate volume. These final results are shown in the table below:

Change from Baseline in Efficacy Endpoints

Endpoint	I-PSS (units)		Maximum Urine Flow Rate (mL/sec)		Prostate Volume (cc)		PSA (ng/mL)	
Visit	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Day 14	—	—	28	3.1** (5.1)	30	–6.5%** (10.9)	28	–1.5% (33.9)
Day 28	29	–7.3** (3.5)	29	3.2** (5.2)	29	–11.2%** (15.2)	29	–17.8%** (25.2)
Day 200	—	—	25	4.2** (5.1)	26	–4.3% (18.4)	26	–14.8%* (27.8)

* p<0.05 versus baseline
** p<0.005 versus baseline
Note: missing observations carried forward for Day 14 and Day 28 endpoints.

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 drug-related adverse events reported by the investigator.

Ongoing Clinical Program

We have initiated two separate multi-center, randomized, placebo controlled, double blinded clinical studies. The first of these was accepted by the FDA as our investigational new drug application, or IND, opening clinical study and is being conducted in the U.S. We completed enrollment in March 2006 in this Phase 2 study that was initiated in June 2005 and are randomizing approximately 200 men with symptomatic BPH to one of five cohorts in a parallel fashion: placebo or one of four doses of TH-070 (5, 25, 50, or 150 mg) to be taken orally once per day for 28 days. The primary objective of this study is to assess the safety of TH-070 and to define the dose response relationship with respect to several measures of efficacy after 28 days of dosing. Standard endpoints and definitions will be used, including prostate size, maximum urine flow rate, PSA, residual volume of urine, and an assessment of each patient's BPH symptoms as measured by the IPSS score. Safety will be assessed using standard safety reporting. Subjects will be followed for three months after they receive their last dose of study drug to assess the durability of response across efficacy variables and long-term safety. At the completion of this study, we expect to be able to understand the dose response relationship of TH-070 in men with symptomatic BPH. This study is not

designed to demonstrate statistically significant differences in efficacy as compared to placebo. We expect to have results from this trial around the beginning of the fourth quarter of 2006.

We also expect to complete enrollment in April 2006 in a Phase 3 study that was initiated in August 2005 in Europe (designated as the "EU Ph 3 study") that has subsequently been expanded to include sites in Canada. This study is randomizing approximately 480 men with symptomatic BPH to one of three cohorts in a parallel fashion: placebo or one of two doses of TH-070 (50 or 150 mg) to be taken orally once per day for twelve weeks. This study design is similar to those that have been used for pivotal studies for alpha blockers. The primary objective of this study is to assess the safety of TH-070 and to assess its efficacy as assessed by IPSS of either dose of TH-070 compared to placebo. Secondary endpoints of efficacy include prostate size, maximum urine flow rate, residual volume of urine, and PSA. Safety will be assessed using standard safety reporting. Subjects will be followed for one month after they receive their last dose of study drug to assess safety. At the completion of this study, we expect to be able to determine whether the administration of either dose of TH-070 daily for twelve weeks is associated with statistically and clinically meaningful differences compared to placebo and if TH-070 is well tolerated in this setting. We expect to have results from this trial around the beginning of the fourth quarter of 2006.

We plan to start three additional supportive trials in 2006. We expect that further efficacy and safety clinical trials will be necessary to achieve marketing approval.

Glufosfamide

Pancreatic Cancer Market Opportunity

The American Cancer Society estimated that 32,180 patients would be diagnosed with pancreatic cancer in the United States in 2005, and approximately 31,800 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. gemcitabine is the standard of care for the first-line therapy of advanced metastatic pancreatic cancer. In 2002, worldwide sales of Gemzar (gemcitabine) for pancreatic cancer were forecast to be $458 million in 2004.

Current Therapies for Cancer

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

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

With respect to pancreatic cancer, current therapies have limited efficacy. The largest published trial of gemcitabine in advanced pancreatic cancer reported a median survival of 5.4 months. In gemcitabine'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 a confirmed objective response as measured by tumor shrinkage.

Potential Advantages of Glufosfamide

Our lead product candidate for cancer, glufosfamide, is a small molecule in clinical development for the treatment of pancreatic cancer. Glufosfamide combines the active part of an approved alkylator, a member of a widely used class of chemotherapy drugs, with a glucose molecule. Because of its glucose component and a tumor cell's increased need for glucose, glufosfamide is preferentially transported into tumors compared to most normal tissues. 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, unless another drug is co-administered.

We believe that the unique mechanism of action of glufosfamide and its demonstrated activity in combination with gemcitabine in animal studies make it well-positioned to be used in combination with gemcitabine. We are developing glufosfamide for pancreatic cancer based on activity seen in previous clinical trials, a known increase in glucose uptake in pancreatic cancer cells and the extreme hypoxia in tumors of this type. Glufosfamide has also shown activity against other tumor types. We believe it may offer an improvement over conventional therapies for the indications where activity has been observed.

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 six years after being treated with glufosfamide alone, this patient remained alive and disease-free. A subsequent study (discussed below) demonstrated that this example is not representative of the activity of glufosfamide for pancreatic cancer 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, and pancreatic cancers, marginal activity against non-small cell lung cancer and no activity for the treatment of glioblastoma.

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

In the Phase 1 and Phase 2 trials, glufosfamide was generally well tolerated, with few drug-related serious adverse events. In particular, glufosfamide's adverse effects on bone marrow and the kidneys were generally reversible without requiring treatment of the side effects. Only 1% of patients developed severe lowering of the

blood platelets, which help to stop bleeding. Toxicity to the kidney, as measured by serum elevation in waste products normally excreted by the kidney, was severe in only 1% of patients. Nausea and vomiting is the most common side effect of glufosfamide treatment. There have been no reports of hemorrhagic cystitis in patients treated with glufosfamide.

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

In December 2005 we completed the Phase 1 portion of a Phase 1/2 dose-escalation study of glufosfamide in combination with gemcitabine for the treatment of advanced solid tumors and pancreatic cancer. The primary objective of the Phase 1 portion of the trial was to evaluate safety and to determine the maximum tolerated dose of glufosfamide when administered in combination with gemcitabine. Glufosfamide in combination with gemcitabine was shown to be well tolerated, no significant interaction between glufosfamide and gemcitabine was shown in the pharmacokinetics analysis and the dose of 4500 mg/m^2 of glufosfamide in combination with gemcitabine was reached. This dose is the dose that is being used in both the Phase 2 stage of this trial of glufosfamide in combination with gemcitabine for first-line treatment of pancreatic cancer and in our ongoing Phase 3 trial of glufosfamide for the second-line treatment of pancreatic cancer.

Ongoing Clinical Programs

We are developing glufosfamide as a single agent for the second-line treatment of metastatic pancreatic cancer, and in combination with gemcitabine 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 gemcitabine. This two-arm trial will compare glufosfamide to best supportive care, because there is no approved second-line treatment for pancreatic cancer. The trial will enroll approximately 300 patients. For its primary endpoint, this trial will compare the survival of patients treated with glufosfamide to patients who received 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 and is statistically persuasive. In addition, glufosfamide for the treatment of second-line 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. We expect to have results from this trial at the end of 2006.

In December 2005, we completed the Phase 1 stage of a Phase 1/2 trial to evaluate glufosfamide in combination with gemcitabine for the first-line treatment of advanced pancreatic cancer patients and began the Phase 2 stage in January 2006. This trial will evaluate up to 28 previously-untreated patients with locally advanced and/or metastatic pancreatic cancer who will receive the standard dose of gemcitabine plus glufosfamide. In addition to safety, the study will investigate the efficacy of glufosfamide in combination with gemcitabine as determined by response rate, duration of response, progression-free survival, overall survival, six- and twelve-month survival and change in serum tumor marker levels. We expect to have early response data at the end of 2006 and six-month survival data in 2007.

Even though our immediate efforts are focused on pancreatic cancer, the results of Phase 1 and Phase 2 clinical trials suggest that glufosfamide may also be useful for the treatment of other cancers. We expect to initiate additional glufosfamide clinical trials for other indications and plan to start at least one of those studies in 2006. Based on human clinical data, the activity of approved alkylators and our understanding of the mechanism of action of glufosfamide, we believe that breast, small cell lung, ovarian and colon cancers, as well as lymphomas and sarcomas, represent the most promising indications.

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 docetaxel to evaluate the safety, blood levels and maximum tolerated dose in patients with solid tumors. Animal studies suggest that 2DG and docetaxel may work together to kill cancer cells with greater efficacy than either drug alone, without increased risk of side-effects. We are developing 2DG based on its specificity for targeting tumor cells and extensive human safety data, as well as 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 600 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 supports the safe use of 2DG in humans, we have not yet obtained human safety data for the cumulative dose or oral administration of 2DG we intend to use in our clinical trials. The FDA may require such data before allowing us to proceed into pivotal clinical trials that will support approval.

We launched a Phase 1 clinical trial of 2DG in January 2004. 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 docetaxel. The study is intended to enroll up to 50 patients with previously treated refractory advanced solid tumors. The study is designed to evaluate the effect of 2DG alone and in combination with docetaxel on tumor growth, and provide a preliminary assessment of efficacy, as assessed by computer tomography. Initial data from this study, reported at American Society of Clinical Oncology, or ASCO, 2005, suggest that 2DG is well tolerated when administered daily for one week every other week, and we intend to evaluate 2DG administered daily, the schedule we believe will ultimately give 2DG the best opportunity to demonstrate efficacy in this setting. We expect to complete this study by year-end 2006.

Provided our safety study yields favorable results, we may initiate at least one Phase 2 study that will be randomized, blinded, multiple-dose studies designed to evaluate the safety and efficacy of 2DG given continuously in combination with chemotherapy. We will choose indications and appropriate combination therapies for our Phase 2 program based on the results of the ongoing Phase 1 trial.

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 identify additional compounds suitable for development as BPH products. Our efforts include 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 BPH and cancer. Key elements of our strategy are to:

- *Develop TH-070, glufosfamide and 2DG successfully.* For TH-070, we have an ongoing Phase 2 trial in the United States and a Phase 3 trial in Europe for the treatment of symptomatic BPH. For glufosfamide, we have an ongoing Phase 3 trial for the second-line treatment of metastatic pancreatic cancer and an ongoing Phase 2 trial for the first-line treatment of inoperable locally advanced or metastatic pancreatic cancer. 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 aggressively, and are also exploring additional indications for these product candidates.
- *Continue to broaden our pipeline by sourcing, identifying, discovering and developing new compounds.* We are actively pursuing research programs to discover and develop novel therapies that address major currently unmet medical needs. We also plan to continue to evaluate additional in-licensing opportunities that build on our expertise and complement our current 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.
- *Execute our commercialization strategy by developing sales and marketing capabilities in selected markets and 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 TH-070, glufosfamide, 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 active pharmaceutical ingredient, or API, and final drug product of TH-070, glufosfamide, 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 establish our own manufacturing facilities.

We believe that we have sufficient TH-070 drug product to conduct and complete our two current BPH clinical trials. We have ordered and received additional TH-070 API that has been formulated into drug product and is available for further clinical trials and related studies.

We currently have sufficient supplies of glufosfamide drug product to conduct our planned clinical trials through November 2006. We are in the process of qualifying an additional vendor to manufacture glufosfamide API. If we experience unexpected delays, or if the API does not meet specifications, we may experience a significant delay in the completion of our pivotal Phase 3 trial.

We believe that we have a sufficient supply of 2DG for our anticipated clinical trials over the next year, although we cannot be certain 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. Additional quantities of API have been ordered and are in the process of being manufactured.

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. 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.

Sales and Marketing

We intend to build our own sales force to market our cancer drugs and to maintain commercial rights to our cancer products in the United States and potentially in Europe. Because the United States cancer market is relatively concentrated, we believe we can effectively target it with a small specialized sales force. We may pursue strategic collaborations to commercialize or co-promote our products for cancer in other territories 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 Agreement

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 our TH-070 product candidate 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, collectively, 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 conducted pursuant to the 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-based Threshold product exceed €50 million. 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 the active ingredient of TH-070 for a purchase price of €75,000. We also granted Acraf a first right to manufacture and supply 75% 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 manufacture and supply right begins in June 2006 and extends for 10 years from the date of the first launch of our first TH-070-based product, 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 15 years from the date of the first launch of our first TH-070-based product in exclusive territories. Acraf's licenses under the agreement extend for 15 years following Acraf's first launch of any product containing the TH-070 active ingredient 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 that cannot be overcome.

Glufosfamide License

In August 2003, we entered into an agreement with Baxter International, Inc., and Baxter Healthcare S.A., or 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 up to mid-single digit 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 agreed with MediBIC on a development plan for glufosfamide for the treatment of pancreatic cancer in certain Asian countries, including Japan, South Korea, India, China, Taiwan and Hong Kong. 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 our 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 a non-exclusive license to use our 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, under a separate but related agreement, an option payment of $250,000. 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.

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 of the glufosfamide product. 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 applications. One United States patent licensed under this agreement has been issued. This patent and the 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 new drug application, or 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 United States 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, 2005, we owned one issued patent, 34 pending United States patent applications; 13 international, or PCT, patent applications; and 72 pending foreign national patent applications; and held exclusive commercial rights to one issued United States patent and 24 issued foreign counterparts of this patent, and one additional foreign patent relating to our glufosfamide product candidate; and

to one issued United States patent and three foreign applications and three United States continuation counterpart applications of this patent relating to our 2DG patent candidate; and to one US patent application, and one counterpart international and two counterpart foreign applications of this application relating to TH-070 analogs.

Intellectual Property Related to TH-070

Our TH-070 product candidate for BPH is protected by one issued United States patent claiming methods of treating BPH, as well as three pending United States continuation patent applications and 16 foreign national counterpart patent applications. The term of any patent that issues on these applications is not expected to lapse until 2024, assuming patent term extension is not available. We have also filed one United States patent application and 13 foreign national counterpart patent applications that broadly claim the use of energolytic agents, agents that disrupt the production of energy, to treat BPH. We have also filed United States, international counterpart, and foreign national counterpart applications relating to TH-070 analogs and prodrugs.

We have also filed patent applications claiming methods for treating and/or preventing other diseases with TH-070 and its analogs. We have filed one United States patent application and two foreign national counterpart patent applications claiming methods for treating certain cancers by administering TH-070 in combination with certain other anti-cancer agents. We have also filed one international patent application and one foreign counterpart patent application claiming methods for preventing prostate cancer by administering TH-070. We have also filed two provisional United States patent applications claiming methods for using TH-070 as adjuvant therapy for, or in place of, a prostatectomy in the treatment of prostate cancer. We have also filed one international patent application claiming methods for treating macular degeneration by administering TH-070 or an analog of TH-070.

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 extension, there can be no assurance that we will obtain such extension. Based on our current clinical timeline, if such an extension were obtained, then we expect that it would be for approximately three years or less in the United States. We also have filed one United States patent application and seven counterpart foreign patent applications describing methods for the identification of patients likely to be most responsive to glufosfamide therapy. We have also filed two international patent applications describing the use of glufosfamide in combination with other agents, including gemcitabine, to treat cancer. In addition, we have filed one United States provisional patent application on a new unit dose form of our glufosfamide product candidate.

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 three pending United States continuation patent applications and three foreign counterpart patent applications claiming the use of 2DG and other glycolytic inhibitors in combination with certain other cancer drugs. The term of any patent that issues on these applications is not expected to lapse until 2020, assuming patent term extension is not available. We have licensed exclusive commercial rights to these patents from the inventors. In addition, we own one issued United States patent that claims methods for administering 2DG to treat cancer, and we have filed one United States continuation patent application of this application and 16 foreign counterpart patent applications that claim methods for dosing, administering, and formulating 2DG to treat cancer. The term of any patent that issues on these applications is not expected to lapse until 2024, assuming patent term extension is not available.

Intellectual Property Related to Our Discovery Research

We have filed three United States patent applications, three international patent applications, and 14 foreign national counterparts of one of the United States patent applications based on our research on hypoxia-activated prodrugs, claiming 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, even for patent applications that have been allowed. Moreover, an issued patent does not guarantee us the right to practice the patented technology or commercialize the patented product. Other 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, 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 and BPH. 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 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, Abbott Laboratories and Astellas Pharma Inc., Cardura®, marketed by Pfizer, and Xatral®, marketed by the sanofi-aventis Group and with 5-alpha reductase inhibitors, including Proscar®, marketed by Merck, and Avodart®, marketed by GlaxoSmithKline. 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 2004 sales of approximately $1.5 billion, and Proscar, which had worldwide 2004 sales of approximately $770 million. Alpha adrenergic receptor blockers, such as Flomax, are believed to 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, abnormal ejaculation, rhinitis and cardiovascular effects such as dizziness, fainting and lightheadedness. 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.

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 Eli Lilly and Company, and 5-flurouracil, or 5-FU, a generic product which is sold by many manufacturers. In 2002, worldwide sales of Gemzar for pancreatic cancer were forecast to be $458 million in 2004. In Gemzar's (gemcitabine) Phase 3 registrational trial, no patient survived beyond two years. In addition, Camptosar®, marketed by Pfizer, Avastin, marketed by Genentech, Inc., Erbitux marketed by Imclone Systems Incorporated and Bristol-Myers Squibb Company, and Taxotere, marketed by the sanofi-aventis Group, are under investigation as possible combination therapies for first-line treatment of pancreatic cancer. Additionally, OSI Pharmaceuticals and Genentech market Tarceva as a combination therapy with gemcitabine for the first-line treatment of pancreatic cancer. Therion Biologics reported that they have completed enrollment in a Phase 3 trial for PANVAC-VF, a vaccine, for the second-line treatment for pancreatic cancer.

Governmental Regulation and Product Approval

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

United States Regulation

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

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

- pre-clinical laboratory and animal tests;
- submission of an 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 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, or cGMP, requirements and preclinical safety tests must be conducted in compliance with FDA and international regulations regarding good laboratory practices, or GLP. The results of the preclinical tests, together with manufacturing information and analytical data, are generally submitted to the FDA as part of an 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 trials, 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 monitor patients to determine effectiveness of the drug candidate and 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 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 10 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 be certain 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 cGMP 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 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.

Anti-Kickback and False Claims Laws

In the United States, we are subject to various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback and false claims laws. The federal Anti-Kickback Law makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, offer, receive or pay any remuneration, directly or indirectly, in exchange for, or to induce, the referral of business, including the purchase, order or prescription of a particular drug, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. Violations of the law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the federal Anti-Kickback Law. Some of these state prohibitions apply to referral of patients for healthcare services reimbursed by any source, not only the Medicare and Medicaid programs. Due to the breadth of these laws, and the potential for additional legal or regulatory change addressing some of our practices, it is possible that our practices or our relationships with physicians might be challenged under anti-kickback laws, which could harm us.

False claims laws prohibit anyone from knowingly presenting, or causing to be presented, for payment to third-party payors (including Medicare and Medicaid) claims for reimbursed items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically

unnecessary items or services. Our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of Medicaid rebate information and other information affecting federal, state and third-party reimbursement of our products, and the sale and marketing of our products, are subject to scrutiny under these laws. In addition, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim. In addition, certain states have enacted laws modeled after the federal False Claims Act. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and suffer a decline in our stock price.

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 patent life 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.

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, 2005, we had 66 employees, including 16 who hold Ph.D. and/or M.D. degrees. Forty-five 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.

Our Corporate Information

We were incorporated in Delaware on October 17, 2001. Our principal executive offices are located at 1300 Seaport Boulevard, Redwood City, California, 94063. Our telephone number is (650) 474-8200.

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 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 website is 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 at www.thresholdpharm.com or by contacting the Investor Relations Department at our corporate offices by calling (650) 474-8200.

ITEM 1A. RISKFACTORS

Risks Related to Our Business

We are substantially dependent upon the success of our TH-070 and glufosfamide 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, TH-070 and glufosfamide, 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 in cancer trials or percentages or results obtained from small scale Phase 2 clinical trials are not necessarily indicative of the results in larger clinical trials.

There can be no assurance that our ongoing clinical trials for symptomatic BPH will confirm results from our Phase 2 trial in Italy, will show that beneficial results of TH-070 will be sustained beyond 28 days, or will

lead to regulatory approval. We completed enrollment in March 2006 in a Phase 2 trial that was initiated in the United States in June 2005 and expect to complete enrollment in April 2006 in a Phase 3 trial that was initiated in August 2005 in several European countries and Canada for this indication; however, we expect regulatory agencies will require additional clinical trials and may require additional preclinical studies to support approval of TH-070 for the treatment of symptomatic BPH. A portion of the preclinical studies were completed by others in the early 1980s in connection with the development of the active ingredient in TH-070 as an anti-cancer agent. If these studies are deemed inadequate, additional studies to satisfy FDA requirements would need to be conducted, which could result in delays in obtaining any regulatory approvals.

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. There can be no assurance that results similar to our Phase 1 and 2 trials 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. The clinical trial we commenced in September 2004 for the second-line treatment of pancreatic cancer is intended to 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. 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.

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 be assured of successfully completing 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 and sites 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 the indication we are currently testing for our glufosfamide product candidate. In addition, we are aware that our planned and future 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 be assured 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 regulatory approval policies 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 second-line 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 lengthened. In addition, our Fast Track designation does not increase the likelihood that glufosfamide will receive regulatory approval for the treatment of second-line 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 or delay 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 by others as a male contraceptive because of its effects on spermatogenesis, fertility and shrinkage of testes in animals. As a consequence, these may be significant side effects that may or may not be reversible in patients treated with TH-070 for BPH. Clinical studies to investigate these side effects can be lengthy and expensive, and may be required prior to additional Phase 3 efficacy studies for TH-070. Furthermore, in clinical trials involving cancer patients at doses significantly higher than the doses of TH-070 currently being investigated for BPH, muscle and testicular pain have been observed. These side effects or others 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. Side effects may prevent or delay regulatory approval or limit market acceptance if our products 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. 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 include 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 we do, 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 or terminate 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.

The FDA and foreign regulatory authorities impose significant restrictions on the indicated uses and marketing of pharmaceutical products.

FDA rules for pharmaceutical promotion require that a company not promote an unapproved drug or an approved drug for an unapproved use. In addition to FDA requirements, regulatory and law enforcement agencies, such as the Department of Health and Human Services' Office of Inspector General and the United States Department of Justice, monitor and investigate pharmaceutical sales, marketing and other practices. For example, sales, marketing and scientific/educational grant programs must comply with the Medicare-Medicaid Anti-Fraud and Abuse Act, as amended, the False Claims Act, as amended, and similar state laws. In recent years, actions by companies' sales forces and marketing departments have been scrutinized intensely to ensure, among other things, that actions by such groups do not qualify as "kickbacks" to healthcare professionals. A "kickback" refers to the provision of any item of value to a healthcare professional or other person in exchange for purchasing, recommending, or referring an individual for an item or service reimbursable by a federal healthcare program. These kickbacks increase the expenses of the federal healthcare program and may result in civil penalties, criminal prosecutions, and exclusion from participation in government programs, any of which would adversely affect our financial condition and business operations. In addition, even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which would also harm our financial condition. Comparable laws also exist at the state level.

We are, and in the future may be, subject to new federal and state requirements to submit information on our open and completed clinical trials to public registries and databases.

In 1997, a public registry of open clinical trials involving drugs intended to treat serious or life-threatening diseases or conditions was established under the Food and Drug Administration Modernization Act, or FDMA, in order to promote public awareness of and access to these clinical trials. Under FDMA, pharmaceutical manufacturers and other trial sponsors are required to post the general purpose of these trials, as well as the eligibility criteria, location and contact information of the trials. Since the establishment of this registry, there has been significant public debate focused on broadening the types of trials included in this or other registries, as well as providing for public access to clinical trial results. A voluntary coalition of medical journal editors has adopted a resolution to publish results only from those trials that have been registered with a no-cost, publicly accessible database, such as www.clinicaltrials.gov. The Pharmaceuticals and Research Manufacturers of America has also issued voluntary principles for its members to make results from certain clinical studies publicly available and has established a website for this purpose. Other groups have adopted or are considering similar proposals for clinical trial registration and the posting of clinical trial results. The state of Maine has enacted legislation, with penalty provisions, requiring the disclosure of results from clinical trials involving drugs marketed in the state, and similar legislation has been introduced in other states. Federal legislation was introduced in the fall of 2004 to expand www.clinicaltrials.gov and to require the inclusion of study results in this registry. In some states, such as New York, prosecutors have alleged that a lack of disclosure of clinical trial information constitutes fraud, and these allegations have resulted in settlements with pharmaceutical companies that include agreements to post clinical trial results. Our failure to comply with any clinical trial posting requirements could expose us to negative publicity, fines, and other penalties, all of which could materially harm our business.

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 the sale of 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, 2005, we had a net loss of $44.4 million, and we had an accumulated deficit of $79.0 million. We do not expect to generate any revenue from the sale of our product candidates at least within the next couple of 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 Phase 2 and Phase 3 clinical trials for TH-070 for the treatment of BPH. In addition, we plan to expand our operations, and will need to expand our infrastructure, hire additional personnel and begin commercialization activities. 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 develop products successfully and market and sell them effectively. 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 TH-070 or glufosfamide product candidates fail to show positive results in our ongoing clinical trials, or we do not receive regulatory approval for either of them, or if these product candidates do not achieve market acceptance even if approved, we may not become profitable. 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.

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 terms and timing of any collaborative, licensing, acquisition or other arrangements that we may establish;
- 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; and
- the costs of establishing sales, marketing and distribution capabilities.

We believe that our cash on hand and marketable securities will be sufficient to fund our projected operating requirements through at least 2007, including our current and planned clinical trials of TH-070, glufosfamide, and 2DG, the initial development of a commercialization effort, general corporate purposes and the support and expansion of our product candidate pipeline. We 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 independently. There can be no assurance that we will be able to enter into any such arrangements on reasonable terms, if at all.

We may need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic and market conditions and other factors, many of which are beyond our control. There can be no assurance that sufficient funds will be available to us when required or on satisfactory terms. If necessary funds are not available, we may have to delay, reduce the scope or eliminate some of our development programs, which could delay the time to market for any or all of our product candidates.

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 establish a sales force to market TH-070 for the treatment of symptomatic BPH. We currently have no experience in selling, marketing or distributing pharmaceutical products and do not have a sales force to do so. Before we can commercialize any products, we must develop our sales, marketing and distribution capabilities, which is an expensive and time consuming process and our failure to do this successfully could delay any product launch. Our efforts to develop internal sales and marketing capabilities could face a number of risks, including:

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

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

Our success depends on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel and on our ability to develop and maintain important relationships with leading academic institutions, clinicians and scientists. We are highly dependent upon our senior management and scientific staff, particularly our Chief Executive Officer, Dr. Harold E. Selick, and our Chief Medical Officer, Dr. Alan B. Colowick. We do not have employment contracts with Drs. Selick or Colowick. The loss of the services of Drs. Selick and Colowick or one or more of our other key employees could delay or have an impact on the successful completion of our clinical trials or the commercialization of our product candidates.

As of December 31, 2005, we had 66 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 are a newly public company, we have little experience complying with public company obligations, including recently enacted changes in securities laws and regulations. Compliance with these requirements will increase our costs and although we have hired additional management and financial resources we still may fail to comply.

We are a small company with limited resources. Prior to our initial public offering in February 2005, we operated as a private company and were not subject to many of the requirements applicable to public companies.

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 control over financial reporting. We expect 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 control 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 control 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 TH-070, glufosfamide 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.

We believe we have sufficient supplies of TH-070 drug product that have been tested and released by Pharmaceutics International, Incorporated for our United States Phase 2 and our European Phase 3 trial of TH-070 for the treatment of BPH. Additionally, for future trials, we have ordered and received TH-070 active pharmaceutical ingredient, or API, from an alternative supplier that has been formulated into drug product. Failure of any of these suppliers to continue to provide acceptable API or drug product could delay clinical trials or commercialization of TH-070, if approved.

Our initial supplies of glufosfamide were prepared by a subsidiary of Baxter International, Inc. and were used to initiate our current clinical trials. We are currently using glufosfamide API and drug product that were manufactured, tested and released by other suppliers and we believe this material will be sufficient through November 2006. We are in the process of qualifying an additional vendor to manufacture glufosfamide API. If we experience unexpected delays, or if the API does not meet specifications, we may experience a significant delay in the completion of our pivotal Phase 3 trial.

We believe that we have a sufficient supply of 2DG for our anticipated clinical trials over the next year, 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 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 increase the manufacturing capacity for any of our product candidates in a timely or economic manner successfully 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, similar foreign regulations and other regulatory 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 are using clinical research organizations to oversee our ongoing TH-070 and glufosfamide clinical trials and expect to use the same or similar organizations for our future 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. Completion of our ongoing studies of TH-070 and glufosfamide are dependent upon the continuing 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 our potential treatment for BPH, TH-070, either outside the United States or 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, when and if approved, TH-070 for the treatment of symptomatic BPH either outside the United States or 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 potential 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 on the composition of the molecules.

TH-070 and 2DG are known compounds that are no longer eligible for patent protection on the composition of the molecules. A patent of this nature, known as 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. once marketed TH-070 in certain European countries for the treatment of cancer, and we cannot prevent its sale for that indication or for any indications where we have not received patent protection. We have an issued U.S. patent for the use of TH-070 for the treatment of BPH and we may obtain patents for TH-070 to treat BPH outside the U.S., but there may be off-label use of competitive products even for our patented indication.

We have an issued U.S. patent for the use of orally administered 2-DG for the treatment of cancer at certain doses and administration schedules, and we have in-licensed one issued patent that covers the treatment of breast cancer with 2DG in combination with paclitaxel or docetaxel. We also have applications related to the issued licensed patent that cover other 2DG combination therapies, but there can be no assurance that any other patent application under this license will be issued. Others may develop and market 2DG for the treatment of cancer, however, if they develop treatments using dosing and administration schedules or combination therapies outside the scope of our patents or in contravention of our patent rights.

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 otherwise 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 patent applications do not result in issued patents, or 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. 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 patent applications or in the patent applications 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 that 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. 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. For glufosfamide, the major European counterparts to the U.S. patent expire in 2009 and the U.S. patent expires in 2014. Patent term extension may not be available for these patents.

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 BPH and cancer 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. 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 sanofi-aventis Group, Eli Lilly and Company, Pfizer and SuperGen and from generic pharmaceutical manufacturers. In particular, our glufosfamide product candidate for pancreatic cancer will compete with Gemzar, marketed by Eli Lilly and Company, and 5-flurouracil, or 5-FU, a generic product which is sold by many manufacturers. In addition, Camptosar®, marketed by Pfizer, Avastin, marketed by Genentech, Inc., Erbitux, marketed by Imclone Systems Incorporated and Bristol-Myers Squibb Company, and Taxotere, marketed by the sanofi-aventis Group, are under investigation as possible combination therapies for first-line treatment of pancreatic cancer. Additionally OSI Pharmaceuticals and Genentech market Tarceva as a combination therapy with gemcitabine for the first-line treatment of pancreatic cancer. Therion Biologics has reported that they have completed enrollment in a Phase 3 trial for PANVAC™-VF, a vaccine, for the 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 and distributed by Boehringer Ingelheim Abbott Laboratories and Astellas Pharma Inc., Cardura®, marketed by Pfizer, and Xatral®, marketed by the sanofi-aventis Group and with 5-alpha reductase inhibitors, including Proscar®, marketed by Merck, and Avodart®, marketed by GlaxoSmithKline. 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 $5 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 us to compete effectively and could adversely affect our profitability.

Reimbursement by a governmental and other third-party payor may depend upon a number of factors, including a governmental or 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 governmental 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 112,896 shares through February 28, 2006. 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 TH-070, glufosfamide 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, patents 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 any strategic alliances or acquisitions we may enter into;
- 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.

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

As of March 17, 2006, our officers, directors and holders of 5% or more of our outstanding common stock beneficially own approximately 49.0% of our common stock. As a result, these stockholders, acting together, will be able to significantly influence all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with the interests of other stockholders, and they may act in a manner that advances their best interests and not necessarily those of other stockholders.

A significant portion of our total outstanding shares have been restricted from immediate resale subsequent to our initial public offering in February 2005 and follow-on offering in October 2005, but these shares are now tradable subject to Rule 144. 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. As of March 17, 2006, 37,284,469 shares of common stock were outstanding. Up to

8,357,624 of those shares are held by affiliates and 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 372,844, 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. 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, where we are incorporated, 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 1B. UNRESOLVED STAFF COMMENTS

None.

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 lease an additional 6,489 square feet of laboratory space in Redwood City, California under an agreement that terminates in February 2010. On February 3, 2006, we entered into a lease for an additional 34,205 square feet of office space at our Redwood City headquarters that terminates in 2011 and extends our lease on the current space to 2011. 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. We are 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 our fiscal year ended December 31, 2005.

PART II

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

Our common stock has been traded on The Nasdaq National Market under the symbol "THLD" since February 4, 2005. Prior to that time there was no public market for our stock. The following table lists quarterly information on the price range of our common stock based on the high and low reported sale prices for our common stock as reported by The Nasdaq National Market for the periods indicated below. These prices do not include retail markups, markdowns or commissions.

	High	Low
Year Ended December 31, 2005:		
First Quarter (from February 4, 2005)	$ 7.50	$5.37
Second Quarter	$ 8.50	$5.40
Third Quarter	$14.09	$7.93
Fourth Quarter	$15.43	$8.77

We estimate that there were approximately 115 holders of record of our common stock as of March 17, 2006.

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.

Use of Proceeds From Sale of Registered Securities

In connection with our initial public offering on February 4, 2005, we sold 6,112,601 shares of our common stock for net offering proceeds to us after deducting expenses totaling $38.1 million. In connection with our offering completed on October 28, 2005, we sold 6,399,222 shares of our common stock for net offering proceeds to us after deducting expenses totaling $62.4 million. During the period covered by this report on Form 10-K, we used approximately $27.1 million of the net proceeds of our initial public offering and follow-on offering, including approximately $22.2 million for the clinical development of glufosfamide, TH-070 and 2DG, $4.3 million for research and development of additional product candidates, and approximately $4.9 million for working capital, capital expenditures and other general corporate purposes. The balance of net offering proceeds has been invested in short-term investment grade securities and cash equivalent instruments.

During the three months ended December 31, 2005, we repurchased 8,059 shares at an average price of $0.33 per share from a former employee upon termination of employment pursuant to our contractual repurchase rights.

ITEM 6. SELECTED FINANCIAL DATA

We are a development stage company. The following selected statement of operations data for the years ended December 31, 2005, 2004, and 2003 and balance sheet data as of December 31, 2005 and 2004 have been derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. The following selected statement of operations data for the period from October 17, 2001 (inception) to December 31, 2001 and the year ended December 31, 2002, and balance sheet data as of December 31, 2003, 2002 and 2001 are derived from our audited financial statements not included in this Annual Report on 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 Annual Report on Form 10-K.

	Years Ended December 31,				Period from October 17, 2001 (date of inception) to December 31, 2001
	2005	2004	2003	2002	
	(In thousands, except per share data)				
Revenue	$ 690	$ —	$ —	$ —	$ —
Operating expenses:					
Research and development (1)	35,991	16,327	6,252	2,179	35
General and administrative (1)	11,235	7,649	2,057	306	201
Total operating expenses	47,226	23,976	8,309	2,485	236
Loss from operations	(46,536)	(23,976)	(8,309)	(2,485)	(236)
Interest and other income, net	2,159	443	65	27	—
Interest expense	(31)	(33)	(59)	—	—
Net loss	(44,408)	(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	$(44,408)	$(23,566)	$(49,165)	$(2,458)	$ (236)
Net loss per common share:					
Basic and diluted	$ (1.63)	$ (20.25)	$(501.68)	$(34.62)	$ (2.13)
Weighted average number of shares used in per common share calculations:					
Basic and diluted	27,173	1,164	98	71	111
(1) Includes employee and non-employee non-cash stock-based compensation of:					
Research and development	$ 5,951	$ 2,960	$ 313	$ 21	$ —
General and administrative	3,470	3,015	753	1	—
Total non-cash stock-based compensation	$ 9,421	$ 5,975	$ 1,066	$ 22	$ —

	As of December 31,				
	2005	2004	2003	2002	2001
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 99,654	$ 28,665	$40,818	$ 6,260	$ 187
Working capital	90,655	21,967	40,177	6,154	2
Total assets	102,101	32,213	41,270	6,726	195
Notes payable, less current portion	151	382	242	—	—
Total liabilities	12,733	8,847	1,126	416	193
Redeemable convertible preferred stock	—	49,839	49,839	8,977	236
Total stockholders' equity (deficit)	89,368	(26,473)	(9,695)	(2,667)	(234)

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 consolidated financial statements and related notes included elsewhere in this Annual Report on 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 Annual Report on 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 cells and abnormally proliferating cells so that the drugs are more efficacious and less toxic to healthy tissues than conventional drugs, thereby providing improvements over current therapies.

Our initial clinical programs focus on product candidates for the treatment of benign prostatic hyperplasia, or BPH, a disease characterized by overgrowth of the prostate, and of cancer. We have three product candidates for these programs, for which we have exclusive worldwide marketing rights:

- TH-070 is our lead product candidate for the treatment of symptomatic BPH. We completed enrollment in March 2006 in a Phase 2 trial that was initiated in the United States in June 2005 and we expect to complete enrollment in April 2006 in a Phase 3 trial that was initiated in Europe in August 2005. Both of these trials are multi-centered, randomized, blinded and placebo controlled trials. We previously completed a single center Phase 2 clinical trial in Italy.
- Glufosfamide is our lead product candidate for cancer. We initiated a pivotal Phase 3 clinical trial of glufosfamide for the second-line treatment of pancreatic cancer in September 2004. We have received a special protocol assessment from the FDA for this trial. Glufosfamide for the second-line treatment of pancreatic cancer has also received FDA Fast Track designation. In January 2006, we initiated the Phase 2 stage of a study of glufosfamide plus gemcitabine for the first-line treatment of advanced solid tumors and pancreatic cancer, after completing a Phase 1 dose-escalating study in patients with advanced solid tumors and pancreatic cancer.
- 2-deoxyglucose, or 2DG, our product candidate for the treatment of solid tumors, is being evaluated in a Phase 1 clinical trial alone and as a combination therapy. 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 generated any revenue from the sale of our product candidates, and, prior to our initial public offering in February 2005, we funded our operations through the private placement of equity securities. In February 2005, we completed our initial public offering that raised net proceeds of approximately $38.1 million, and in October 2005, we completed an offering of common stock that raised net proceeds of $62.4 million. As of December 31, 2005 we had cash, cash equivalents, and marketable securities of $99.7 million, which is expected to last through at least 2007. We believe we have sufficient funds to complete our current and planned trials of TH-070, glufosfamide and 2DG. The net loss for the year ended December 31, 2005 was $44.4 million and the cumulative net loss since our inception through December 31, 2005 was $79.0 million.

We expect our net losses to increase primarily due to ongoing and planned clinical trial activities and to prepare for potential commercialization. As we continue to advance our product candidates through development,

we expect our research and development expenses to increase significantly, as we continue our pivotal Phase 3 clinical trial of glufosfamide and our Phase 3 and Phase 2 trials for TH-070 for the treatment of symptomatic BPH as well as start enrollment in additional trials. These clinical trials involve a greater number of patients, are conducted at multiple sites and in various countries, are conducted over a longer period of time and require greater quantities of drug product. Costs associated with these clinical trials are likely to increase on an annual basis and may fluctuate significantly from period to period based largely on clinical trial activities. These costs could even decrease from quarter to quarter as we complete enrollment and patient treatment in current clinical trials. Additionally, we are expanding our infrastructure and facilities, and are hiring additional personnel, including clinical development, research, commercial operations and administrative personnel. We are unable to predict when, if ever, we will be able to commence sales of any product.

Revenue

We have not generated any revenue from the sale of our product candidates since our inception and do not expect to generate any revenue from the sale of our product candidates at least within the next couple of years. In 2005, we recognized $0.7 million in revenue related to a $5.0 million upfront payment received in connection with a 2004 agreement with MediBIC Co., Ltd., or MediBIC, for the development of glufosfamide in Japan and several other Asian countries.

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 consultants and contractors in many of these areas. 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 annual 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, 2005, we spent an aggregate of $60.8 million on research and development expenses, including non-cash stock-based compensation expense.

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, including non-cash stock-based compensation, 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, initiate commercialization activities and as a result of incurring costs associated with being a public company. From inception through December 31, 2005, we spent an aggregate of $21.4 million on general and administrative expenses, including non-cash stock-based compensation expense.

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 $0.5 million, $20.4 million and $2.3 million for the years ended December 31, 2005, 2004 and 2003, respectively. This expense, which is a non-cash charge, has been amortized over the period in which the options vest, which is generally four years. The amortization of this expense recognized for the years ended December 31, 2005, 2004 and 2003 was $5.3 million, $5.3 million and $0.8 million, respectively. Beginning January 1, 2006, we are required to account for stock-based compensation using the fair value method prescribed by SFAS No. 123 "*Share-Based Payment.—An Amendment of FASB Statements No. 123 and 95"*("SFAS No. 123R"), issued by the Financial Accounting Standards Board in December 2004. Refer to the discussion below under ***Recent Accounting Pronouncements***.

We account for equity instruments issued to non-employees in accordance with the provisions of SFAS No. 123 and Emerging Issues Task Force, or 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 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 $4.1 million, $0.7 million and $0.3 million of stock-based compensation expense during the years ended December 31, 2005, 2004 and 2003, respectively.

Results of Operations for the Years Ended December 31, 2005 and 2004

Revenue

For the year ended December 31, 2005, we recognized $0.7 million in revenue related to a $5.0 million upfront payment received in connection with a 2004 agreement with MediBIC for the development of glufosfamide in Japan and several other Asian countries. The payment was contingent upon the finalization of the clinical development plan, which occurred in July 2005. Revenue is being recognized on a straight-line basis over the estimated development period, currently estimated to be through 2008. We are responsible for all development activities under this agreement.

Research and Development

Research and development expenses were $36.0 million for the year ended December 31, 2005 compared to $16.3 million for the year ended December 31, 2004. The $19.7 million increase in expenses is due to a $12.2 million increase in clinical and development expenses, a $3.4 million increase in expenses associated with higher staffing levels, a $3.0 million increase in non-cash stock-based compensation expense and a $1.1 million increase in expenses related to new facilities.

Research and development expenses associated with TH-070 were $13.9 million for 2005 compared to $3.3 million for 2004. This $10.6 million increase in expenses was primarily due to the initiation of our Phase 2 United States and Phase 3 European trials and an increase in staffing and related expenses. Research and development expenses associated with glufosfamide were $12.0 million and $7.5 million for 2005 and 2004, respectively. This increase is primarily due to expenses associated with the Phase 3 clinical trial. Research and development expenses associated with 2DG were $2.5 million and $2.8 million for 2005 and 2004, respectively. The decrease is primarily attributable to a reduction in 2DG project staffing and related costs. Discovery research and development expenses were $7.6 million and $2.7 million for 2005 and 2004, respectively. The increase was primarily due to increases in staffing and related costs to support expansion of our discovery research program.

We expect to continue to devote substantial resources to research and development in future periods as we continue our current clinical trials and start additional trials. Research and development expenses will likely increase on an annual basis but may fluctuate from period to period based largely on clinical trial activities. These costs could even decrease from quarter to quarter as we complete enrollment and patient treatment in current clinical trials.

General and Administrative

General and administrative expenses were $11.2 million and $7.6 million for the years ended December 31, 2005 and 2004, respectively. The $3.6 million increase in general and administrative expenses primarily reflects additional expenses associated with becoming a public company in 2005, including $1.2 million of higher legal fees, insurance premiums, and consulting services; and $1.2 million of expenses related to higher staffing levels. Additionally, the increase in general and administrative expenses in 2005 compared to 2004 was due to $0.7 million of increased patent expenses and a $0.5 million increase in non-cash stock-based compensation expenses.

We expect our general and administrative expenses to continue to increase due to additional administrative and infrastructure costs as well as costs associated with implementing procedures for compliance with Section 404 of the Sarbanes-Oxley Act of 2002.

Interest and Other Income

Interest income for the year ended December 31, 2005 was $2.2 million compared to $0.4 million for the year ended December 31, 2004. The increase was due to greater invested cash balances due to proceeds received from our initial public offering completed in February 2005 and our follow-on offering completed in October 2005, as well as higher average interest rates in 2005.

Interest Expense

Interest expense for the years ended December 31, 2005 and 2004 was $31,000 and $33,000, respectively, reflecting the declining balance of our note payable.

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 in 2004 was due primarily to increases of $2.5 million for clinical trial costs, $1.9 million 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 $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 $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 $2.7 million for the year ended December 31, 2004 and $1.6 million for the year ended December 31, 2003. The increase in discovery research expenses was primarily due to increased staffing.

General and Administrative

General and administrative expenses were $7.6 million for the year ended December 31, 2004 compared to $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.

Interest Income

Interest income for the year ended December 31, 2004 was $0.4 million compared to $65,000 for the year ended December 31, 2004. 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

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 of debt issuance costs associated with warrants issued in conjunction with our 2003 line of credit.

Liquidity and Capital Resources

We have incurred net losses since inception through December 31, 2005 of $79.0 million. We have not generated any revenues and do not expect to generate revenue from the sale of product candidates at least within the next couple of years. From inception until our initial public offering in February 2005, we funded our operations primarily through the private placement of our preferred stock. In February 2005, we completed our initial public offering of 6,112,601 shares of our common stock, raising net proceeds of $38.1 million. In October 2005, we completed a public offering of 6,399,222 shares of our common stock for net proceeds of $62.4 million.

At December 31, 2005, we had cash and cash equivalents of $74.9 million compared to $14.3 million and $40.6 million at December 31, 2004 and 2003, respectively. In addition, we had $24.7 million in marketable securities at December 31, 2005, compared to $14.3 million and $0.2 million at December 31, 2004 and 2003, respectively, which were also available to fund operations.

Net cash used in operating activities for the years ended December 31, 2005, 2004 and 2003 was $29.9 million, $10.8 million and $6.7 million, respectively. For the year ended December 31, 2005, cash used in operations resulted from the net loss for the year after adding back non-cash charges for stock-based compensation expense, additional accruals for clinical and development expenses and personnel-related expenses, depreciation expense and deferred revenue. For the year ended December 31, 2004 cash used in operations was attributable 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 our development agreement with MediBIC. 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.

Net cash used in investing activities of $11.5 million, $15.4 million and $0.2 million for the years ended December 31, 2005, 2004 and 2003, respectively, was primarily used for purchases of marketable securities of $38.9 million and $38.2 million in 2005 and 2004, respectively, capital spending of $1.2 million, $1.0 million and $0.2 million in 2005, 2004 and 2003, respectively, partially offset in 2005 and 2004 by sales of marketable securities of $28.4 million and $24.0 million in 2005 and 2004, respectively.

Net cash provided by financing activities was $102.0 million for the year ended December 31, 2005 primarily from the two public offerings completed during the year: our initial public offering that was completed

in February and raised $38.1 million of net proceeds, and our follow-on offering that was completed in October and raised $62.4 million of net proceeds. 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, which were partially offset by borrowings under a loan agreement, net of repayments. Net cash provided by financing activities was $41.3 million for the year ended December 31, 2003, which was primarily attributable to the sale of redeemable convertible preferred stock.

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.

We expect 2006 cash requirements to be in the range of $48 to $55 million. We believe that our cash on hand and marketable securities as of December 31, 2005, will be sufficient to fund our projected operating requirements through at least 2007, including our current and planned clinical trials of TH-070, glufosfamide and 2DG, the research and discovery efforts towards additional product candidates, the initial development of a commercialization effort, working capital and general corporate purposes. We 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. Additionally, we may need to raise additional capital or incur indebtedness to continue to fund our operations in the future. Our ability to raise additional funds will depend on financial, economic, market conditions and other factors, many of which are beyond our control. There can be no assurance that sufficient funds will be available to us when required or on satisfactory terms. If necessary funds are not available, we may have to delay, reduce the scope or eliminate some of our research and development, which could delay the time to market for any of our product candidates.

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. As of December 31, 2004, we had borrowed the full amount under this facility, which is being repaid over a 36-month period from the dates of borrowing. These borrowings bear interest at an average rate of 5.8% per year at December 31, 2005. At December 31, 2005 the amount due under this facility was $0.4 million. The financial covenant in this agreement requires us to maintain the lower of 85% of our total cash and cash equivalents or $10.0 million at Silicon Valley Bank. At December 31, 2005, we were in compliance with our covenant.

In August 2004, we entered into a noncancelable facilities sublease agreement for approximately 34,205 square feet that expires on February 28, 2010. On April 1, 2005, we entered into a noncancelable facility operating lease for approximately 6,489 square feet of laboratory space, which also expires in February 2010.

In February 2006, we entered into a lease for an additional 34,205 square feet of space and increased the lease term for the existing 34,205 square feet of space located at our headquarters in Redwood City, California. The lease is for a period of 66 months, and will begin on April 1, 2006 with respect to the additional square footage and on March 1, 2010 with respect to the existing square footage. The lease will expire, unless otherwise terminated under the terms of the lease, on September 30, 2011. The aggregate rent for the term of the lease is approximately $4.8 million. In addition, the lease requires us to pay certain taxes, assessments, fees and other costs and expenses associated with the premises as well as a customary management fee. We will also be responsible for the costs of certain tenant improvements associated with the leased space. In connection with the lease, we will furnish a letter of credit in customary form to the landlord in an amount of approximately $0.3 million. We intend to borrow up to approximately $4.0 million for leasehold improvements related to this additional leased space and other capital expenditures.

Our major outstanding contractual obligations consist of amounts due under our financing and lease agreements, and purchase commitments. Contractual obligations and related scheduled payments as of December 31, 2005, are as follows (in thousands):

	Within one year	One to three years	Four to five years	After five years	Total
Facilities sublease and lease	$ 540	$ 1,911	$ 114	$ —	$2,565
Notes payable, principal and interest	246	156	—	—	402
Purchase commitments	106	—	—	—	106
Total	$ 892	$ 2,067	$ 114	$ —	$3,073

In November 2004, we entered into an agreement with MediBIC to develop glufosfamide in Japan and several other Asian countries, and received an upfront payment of $5.0 million contingent upon the finalization of the clinical development plan. In July 2005, we finalized the development plan with MediBIC and began recognizing revenue from the upfront payment on a straight-line basis over the development period, currently estimated to be through 2008. We are responsible for all development activities under this agreement. We will also be required to make royalty payments upon product commercialization. We may terminate the agreement at any time by making certain payments ranging from $5.25 million to $15.0 million, depending on the stage of development.

In August 2003, we entered into an agreement with Baxter International 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 $0.1 million and a $0.1 million 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 up to mid-single digit 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 $0.7 million 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 $0.4 million, 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. Future aggregate milestone payments under this agreement could total €1.8 million (approximately $2.1 million based on the exchange rate at December 31, 2005).

Off-Balance Sheet Arrangements

As of December 31, 2005, 2004 and 2003, 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.

Income Taxes

We incurred net operating losses for the years ended December 31, 2005, 2004, and 2003 and, accordingly, we did not pay any federal or state income taxes. As of December 31, 2005, we had accumulated approximately $61.0 million in both federal and state net operating loss carryforwards to reduce future taxable income. If not utilized, our federal and state net operating loss carryforwards begin to expire in 2021 and 2013 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, 2005, we had research credit carryforwards of approximately $1.3 million and $1.2 million for federal and California state income tax purposes, respectively. If not utilized, the federal carryforwards will expire in 2021 through 2025. 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.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated 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 consolidated financial statements included in this Annual Report on Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our consolidated 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 our common stock for options granted through the date of the initial public offering in February 2005 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 period from January 1, 2005 through the date of our initial public offering and the years ended December 31, 2004 and 2003. As disclosed more fully in Note 9 of the notes of our consolidated financial statements, we granted stock options and restricted common stock with exercise prices ranging from $0.16 to $0.53 per share during the period from January 1, 2005 through the date of our initial public offering and the years ended December 31, 2004 and 2003. 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 were not publicly traded before our initial public offering in February 2005, 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

Most of our preclinical and clinical trials are performed by third party contract research organizations, or CROs, and clinical supplies are manufactured by contract manufacturing organizations, or CMOs. Invoicing from these third parties may be monthly based upon services performed or based upon milestones achieved. We accrue these expenses based upon our assessment of the status of each study and the work completed, and upon information obtained from the CROs and CMOs. Our estimates are dependent upon the timeliness and accuracy of data provided by the CROs and CMOs regarding the status and cost of the studies, and may not match the actual services performed by the organizations. This could result in adjustments to our research and development expenses in future periods. To date we have had no significant adjustments.

Marketable Securities

We classify all of our marketable securities as available-for-sale. We carry these investments at fair value, based on quoted market 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.

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

Share-based Payment: 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 the same as any other form of compensation by recognizing the related cost in the statement of operations. This pronouncement eliminates the alternate method of accounting 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. We will adopt SFAS 123R using the modified prospective application on January 1, 2006. Adoption of this statement could have a significant impact on our financial statements as we will be required to expense the fair value of our stock option grants and stock purchases under our employee stock purchase plan rather than disclose the impact on our net loss within our footnotes. The impact of adoption of SFAS 123R on our future operating results has not yet been determined and will depend, among other factors, upon levels of stock-based awards and the volatility of our stock price. We are in the process of determining the impact of this standard on our financial statements.

Accounting Changes and Error Corrections: On June 7, 2005, the FASB issued Statement No. 154, Accounting Changes and Error Corrections, a replacement of APB Opinion No. 20, *Accounting Changes,* and Statement No. 3*, Reporting Accounting Changes in Interim Financial Statements.* Statement 154 changes the requirements for the accounting for and reporting of a change in accounting principle. Previously, most voluntary changes in accounting principles required recognition via a cumulative effect adjustment within net income of the period of the change. Statement 154 requires retrospective application to prior periods' financial statements, unless it is impracticable to determine either the period-specific effects or the cumulative effect of the change. Statement 154 is effective for accounting changes made in fiscal years beginning after December 15, 2005; however, the Statement does not change the transition provisions of any existing accounting pronouncements. We do not believe adoption of Statement 154 will have a material impact on our financial statements.

Other-Than-Temporary Impairment of Certain Investments: In November 2005, the FASB issued FASB Staff Position Nos FAS 115-1 and FAS 124-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments" ("FSP FAS 115-1"), which provides guidance on determining when investments in certain debt and equity securities are considered impaired, whether that impairment is other-than-temporary, and on measuring such impairment loss. FSP FAS 115-1 also includes accounting considerations subsequent to the recognition of an other-than temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. FSP FAS 115-1 is required to be applied to reporting periods beginning after December 15, 2005. We are required to adopt FSP FAS 115-1 in the first quarter of fiscal 2006. We do not expect that the adoption of the statement will have a material impact on our financial statements.

ITEM 7A. QUANTITATIVEAND QUALITATIVE DISCLOSURE OF MARKET RISKS

Interest Rate Risk. Our exposure to market risk for changes in interest rates relates to our cash equivalents on deposit in highly liquid money market funds and investments in short-term marketable securities. The primary objective of our cash investment activities is to preserve principal while at the same time maximizing the income we receive from our invested cash without significantly increasing risk of loss. We invest in high-quality financial instruments, which currently have an average maturity of less than one year. We do not use derivative financial instruments in our investment portfolio. Our cash and investments policy emphasizes liquidity and preservation of principal over other portfolio considerations. Our investment portfolio is subject to interest rate risk and will fall in value if market interest rates rise. However, due to the short duration of our investment portfolio we believe an immediate 10% change in the interest rates would not be material to our financial condition or results of operations.

In addition, we do not have any material exposure to foreign currency rate fluctuations as we operate primarily in the United States. Although we conduct some clinical and safety studies, and manufacture some active pharmaceutical product with vendors outside the United States, most of our transactions are denominated in U.S. dollars.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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

Report of Independent Registered Public Accounting Firm

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

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of stockholders' equity (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, 2005 and 2004, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, and cumulatively for the period from October 17, 2001 (date of inception) to December 31, 2005, 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 27, 2006

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

	December 31,	
	2005	2004
ASSETS		
Current assets:		
Cash and cash equivalents	$ 74,947	$ 14,339
Marketable securities	24,707	14,326
Prepaid expenses and other current assets	563	1,604
Restricted cash	—	85
Total current assets	100,217	30,354
Property and equipment, net	1,667	1,667
Restricted cash	192	192
Other assets	25	—
Total assets	$102,101	$ 32,213
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 1,237	$ 1,550
Accrued clinical and development expenses	4,500	444
Accrued liabilities	2,158	1,062
Deferred revenue, current portion	1,437	—
Notes payable, current portion	230	331
Advance on research and development contract (Note 7)	—	5,000
Total current liabilities	9,562	8,387
Deferred revenue, less current portion	2,873	—
Notes payable, less current portion	151	382
Deferred rent	147	78
Total liabilities	12,733	8,847
Commitments and contingencies (Note 7)		
Redeemable convertible preferred stock, $0.001 par value:		
Authorized: None and 33,886,484 shares at December 31, 2005 and 2004, respectively.		
Issued and outstanding: None and 33,848,484 shares at December 31, 2005 and 2004, respectively.	—	49,839
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value:		
Authorized: 2,000,000 shares; No shares issued and outstanding	—	—
Common stock, $0.001 par value:		
Authorized: 150,000,000 shares; Issued and outstanding: 37,231,572 and 3,690,567 shares at December 31, 2005 and 2004, respectively.	37	4
Additional paid-in capital	179,634	24,619
Deferred stock-based compensation	(11,356)	(16,637)
Accumulated other comprehensive income	24	104
Deficit accumulated during the development stage	(78,971)	(34,563)
Total stockholders' equity (deficit)	89,368	(26,473)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$102,101	$ 32,213

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

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

	Years Ended December 31,			Cumulative Period from October 17, 2001 (date of inception) to December 31, 2005
	2005	2004	2003	
Revenue	$ 690	$ —	$ —	$ 690
Operating expenses:				
Research and development	35,991	16,327	6,252	60,784
General and administrative	11,235	7,649	2,057	21,448
Total operating expenses	47,226	23,976	8,309	82,232
Loss from operations	(46,536)	(23,976)	(8,309)	(81,542)
Interest and other income, net	2,159	443	65	2,694
Interest expense	(31)	(33)	(59)	(123)
Net loss	(44,408)	(23,566)	(8,303)	(78,971)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	(40,862)	(40,862)
Net loss attributable to common stockholders	$ (44,408)	$ (23,566)	$ (49,165)	$ (119,833)
Net loss per common share:				
Basic and diluted	$ (1.63)	$ (20.25)	$ (501.68)	
Weighted average number of shares used in per common share calculations:				
Basic and diluted	27,173	1,164	98	

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

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
FOR THE PERIOD
FROM OCTOBER 17, 2001 (DATE OF INCEPTION) TO DECEMBER 31, 2005
(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' Equity (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)

THRESHOLD PHARMACEUTICALS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)—(Continued)
FOR THE PERIOD
FROM OCTOBER 17, 2001 (DATE OF INCEPTION) TO DECEMBER 31, 2005
(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' Equity (Deficit)
	Shares	Amount					
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)
Issuance of common stock in an initial public offering for cash of $7.00, per share, net of issuance costs of $4.6 million	6,112,601	6	38,129	—	—	—	38,135
Issuance of common stock for cash of $10.46 per share, net of issuance costs of $4.5 million	6,399,222	6	62,389	—	—	—	62,395
Issuance of common stock pursuant to exercise of warrants	19,269	—	—	—	—	—	—
Conversion of convertible preferred stock upon initial public offering	20,552,812	21	49,818	—	—	—	49,839
Issuance of common stock pursuant to stock plans	508,626	—	557	—	—	—	557
Deferred stock-based compensation, net of cancellations	—	—	3,321	(3,321)	—	—	—
Reversal of deferred stock-based compensation related to employee terminations	—	—	(2,862)	2,862	—	—	—
Amortization of deferred stock-based compensation	—	—	(416)	5,740	—	—	5,324
Non-employee stock-based compensation	—	—	4,097	—	—	—	4,097
Repurchase of unvested common stock	(51,525)	—	(18)	—	—	—	(18)
Components of other comprehensive income (loss):							
Change in unrealized gain (loss) on marketable securities	—	—	—	—	(80)	—	(80)
Net loss	—	—	—	—	—	(44,408)	(44,408)
Comprehensive loss							(44,488)
Balances, December 31, 2005	37,231,572	$ 37	$ 179,634	$ (11,356)	$ 24	$ (78,971)	$ 89,368

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

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

	Years Ended December 31,			Cumulative Period from October 17, 2001 (date of inception) to December 31, 2005
	2005	2004	2003	
Cash flows from operating activities:				
Net loss	$ (44,408)	$ (23,566)	$ (8,303)	$ (78,971)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation	573	143	90	817
Stock-based compensation expense	9,421	5,975	1,066	16,484
Amortization of debt issuance costs	—	10	34	44
Loss on disposal of property and equipment	—	—	—	5
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(272)	(189)	152	(589)
Accounts payable	257	699	(32)	1,237
Accrued clinical and development expenses	4,057	227	209	4,500
Accrued liabilities	1,114	823	125	2,158
Deferred rent	69	78	—	147
Deferred revenue	(690)	5,000	—	4,310
Net cash used in operating activities	(29,879)	(10,800)	(6,659)	(49,858)
Cash flows from investing activities:				
Acquisition of property and equipment	(1,162)	(1,022)	(218)	(2,489)
Acquisition of marketable securities	(38,874)	(38,199)	—	(71,369)
Proceeds from sales of marketable securities	28,413	24,023	—	46,686
Restricted cash	85	(162)	—	(192)
Net cash used in investing activities	(11,538)	(15,360)	(218)	(27,364)
Cash flows from financing activities:				
Proceeds from redeemable convertible preferred stock, net	—	—	40,862	49,839
Proceeds from issuance of common stock, net of offering expenses	102,357	(415)	1	101,949
Proceeds from issuance of notes payable	—	490	510	1,000
Repayment of notes payable	(332)	(185)	(102)	(619)
Net cash provided by (used in) financing activities	102,025	(110)	41,271	152,169
Net increase (decrease) in cash and cash equivalents	60,608	(26,270)	34,394	74,947
Cash and cash equivalents, beginning of period	14,339	40,609	6,215	—
Cash and cash equivalents, end of period	$ 74,947	$ 14,339	$ 40,609	$ 74,947
Supplemental disclosures:				
Cash paid for interest	$ 31	$ 33	$ 14	$ 78
Non-cash investing and financing activities:				
Deferred stock-based compensation	$ 459	$ 20,385	$ 2,332	$ 23,201
Conversion of redeemable convertible preferred stock	$ 49,839	$ —	$ —	$ 49,839
Deferred offering expenses in connection with IPO	$ (1,287)	$ 1,287	$ —	$ —
Change in unrealized gain in marketable securities	$ (80)	$ (59)	$ 164	$ 24
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
Accrued cost of acquisition of property and equipment	$ (589)	$ 589	$ —	$ —

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

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

NOTE 1—SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Description of Operations and Basis of Presentation

Threshold Pharmaceuticals, Inc. (the "Company") was incorporated in the State of Delaware on October 17, 2001. The Company is a biotechnology company focused on the discovery, development and commercialization of small molecule therapeutics for the potential treatment of benign prostatic hyperplasia (BPH) and cancer. The Company has product candidates in middle-and late-stage development as well as discovery and since inception, has devoted substantially all of its time and efforts to performing research and development, raising capital and recruiting personnel.

In June 2005, the Company formed a wholly-owned subsidiary, THLD Enterprises (UK), Limited in the United Kingdom in connection with conducting clinical trials in Europe. As of December 31, 2005, there has been no financial activity related to this entity.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America and include the accounts of the Company and its wholly owned subsidiary, and reflect the elimination of intercompany accounts and transactions.

The Company believes that its cash on hand and marketable securities as of December 31, 2005, will be sufficient to fund its projected operating requirements through at least 2007, including its current and planned clinical trials of TH-070, glufosfamide and 2DG, the research and discovery efforts towards additional product candidates, the initial development of a commercialization effort, working capital and general corporate purposes. The Company intends to seek funds through arrangements with collaborators or others that may require it to relinquish rights to certain product candidates that it might otherwise seek to develop or commercialize independently. Additionally, the Company may need to raise additional capital or incur indebtedness to continue to fund its operations in the future. The Company's ability to raise additional funds will depend on financial, economic, market conditions and other factors, many of which are beyond its control. There can be no assurance that sufficient funds will be available to the Company when required or on satisfactory terms. If necessary funds are not available, the Company may have to delay, reduce the scope or eliminate some of its research and development, which could delay the time to market for any of its product candidates.

Use of Estimates

The preparation of consolidated 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 consolidated 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 one certificate of deposit held at a financial institution that serves as collateral for the Company's facility sublease agreement.

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' equity (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.

At December 31, 2004, marketable securities included auction rate securities that were 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 were classified as marketable securities at December 31, 2004. The Company did not have investments in auction rate securities at December 31, 2005.

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, 2005 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 financial institutions 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.

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 ("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, 2005, the Company has not incurred any such impairment losses.

Comprehensive income (loss)

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

Revenue Recognition

The Company recognizes revenue in accordance with SFAS No. 68 "Research and Development Arrangements," Staff Accounting Bulletin No. 104 "Revenue Recognition" and Emerging Issues Task Force Issue 00-21 "Revenue Arrangements with Multiple Deliverables". In connection with the Company's agreement with MediBIC, the Company recognizes revenue from non-refundable, upfront payment ratably over the term of its performance under the agreements. The upfront payment received, pending recognition as revenue, is recorded as deferred revenue and classified as a short-term or long-term liability on the balance sheet to be amortized over the period of deferral.

Research and development expenses

Research and development expenses are charged to research and development expense as incurred. Research and development expenses consist of salaries and benefits, laboratory supplies, consulting fees and fees paid to third party contract research and manufacturing organizations.

Preclinical and Clinical Trial Accruals

Most of the Company's preclinical and clinical trials are performed by third party contract research organizations (CROs), and clinical supplies are manufactured by contract manufacturing organizations (CMOs). Invoicing from these third parties may be monthly based upon services performed or based upon milestones achieved. The Company accrues these expenses based upon its assessment the status of each study and the work completed, and upon information obtained from the CROs and CMOs. The Company's estimates are dependent upon the timeliness and accuracy of data provided by the CROs and CMOs regarding the status and cost of the studies, and may not match the actual services performed by the organizations. This could result in adjustments to the Company's research and development expenses in future periods. To date the Company has had no significant adjustments.

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 has one reportable segment and uses one measurement of profitability to manage its business. All long-lived assets are maintained in the United States of America.

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,		
	2005	2004	2003
Net loss attributable to common stockholders, as reported	$(44,408)	$(23,566)	$(49,165)
Add: Employee stock-based compensation included in reported net loss	5,324	5,294	810
Deduct: Employee total stock-based compensation determined under fair value method	(7,100)	(3,601)	(815)
Pro forma net loss attributable to common stockholders	$(46,184)	$(21,873)	$(49,170)
Net loss attributable to common stockholders per common share, basic and diluted:			
As reported	$ (1.63)	$ (20.25)	$(501.68)
Pro forma	$ (1.70)	$ (18.79)	$(501.73)

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

Prior to the closing of the Company's initial public offering, the fair value of each option was estimated using the minimum value method. Following the offering, the value of each employee option and each employee purchase right under the Employee Stock Purchase Plan, which started in February 2005, has been estimated at the date of the grant using the Black-Scholes model, assuming the following weighted-average assumptions:

	2005	2004	2003
Employee Stock Options:			
Weighted average risk-free interest rate	3.66%	2.77%	1.98%
Expected life (in years)	4	4	4
Dividend yield	—	—	—
Volatility (1)	68%	—	—
Employee Stock Purchase Plan (ESPP):			
Weighted average risk-free interest rate	3.19%	—	—
Expected life (in years)	0.5	—	—
Dividend yield	—	—	—
Volatility	72%	—	—

(1) Applied to grants after the initial public offering in February 2005. Grants prior to the initial public offering were valued under the minimum value method, which assumes zero volatility.

The grant date weighted average fair value per share of options granted during the years ended December 31, 2005, 2004 and 2003 was $7.35, $9.01 and $3.47, 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

Share-based Payment: In December 2004, the FASB issued SFAS No. 123R "*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 the same as any other form of compensation by recognizing the related cost in the statement of operations. This pronouncement eliminates the alternate method of accounting 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. The Company will adopt FAS 123R using the modified prospective application method on January 1, 2006. Adoption of this statement could have a significant impact on the Company's financial statements as the Company will be required to expense the fair value of its stock option grants and stock purchases under the Company's employee stock purchase plan rather than disclose the impact on the Company's net loss within our footnotes, as is the current practice. The impact of adoption of SFAS 123R on the Company's future operating results has not yet been determined and will depend, among other factors, upon levels of stock-based awards and the volatility of the Company's stock price. The Company is in the process of determining the impact of this standard on its financial statements.

Accounting Changes and Error Corrections: On June 7, 2005, the FASB issued Statement No. 154,*Accounting Changes and Error Corrections*, a replacement of APB Opinion No. 20, *Accounting Changes*, and Statement No. 3, *Reporting Accounting Changes in Interim Financial Statements*. Statement 154 changes the requirements for the accounting for and reporting of a change in accounting principle. Previously, most voluntary changes in accounting principles required recognition via a cumulative effect adjustment within net income of the period of the change. Statement 154 requires retrospective application to prior periods' financial statements, unless it is impracticable to determine either the period-specific effects or the cumulative effect of the change. Statement 154 is effective for accounting changes made in fiscal years beginning after December 15, 2005; however, the Statement does not change the transition provisions of any existing accounting pronouncements. The Company does not believe adoption of Statement 154 will have a material impact on its financial statements.

Other-Than-Temporary Impairment of Certain Investments: In November 2005, the FASB issued FASB Staff Position Nos FAS 115-1 and FAS 124-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments" ("FSP FAS 115-1"), which provides guidance on determining when investments in certain debt and equity securities are considered impaired, whether that impairment is other-than-temporary, and on measuring such impairment loss. FSP FAS 115-1 also includes accounting considerations subsequent to the recognition of an other-than temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. FSP FAS 115-1 is required to be applied to reporting periods beginning after December 15, 2005. The Company is required to adopt FSP FAS 115-1 in the first quarter of 2006. The Company does not expect that the adoption of the statement will have a material impact on its financial statements.

NOTE 2—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 outstanding 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,		
	2005	2004	2003
Numerator:			
Net loss	$(44,408)	$(23,566)	$ (8,303)
Dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	(40,862)
Net loss attributable to common stockholders	(44,408)	$(23,566)	$(49,165)
Denominator:			
Weighted-average number of common shares outstanding	29,098	2,335	183
Less: Weighted-average shares subject to repurchase	(1,925)	(1,171)	(85)
Weighted-average number of common shares outstanding used in computing basic and diluted net loss per common share	27,173	1,164	98
Basic and diluted net loss per common share	$ (1.63)	$ (20.25)	$(501.68)

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,		
	2005	2004	2003
Redeemable convertible preferred stock	—	20,553	20,553
Options to purchase common stock	926	447	1,791
Common stock subject to repurchase	1,475	2,069	76
Shares issuable related to the ESPP	40	—	—
Warrants to purchase redeemable convertible preferred stock	—	38	38

NOTE 3—MARKETABLE SECURITIES:

The Company invests in highly-liquid, investment-grade securities. The following is a summary of the Company's available-for-sale securities at December 31, 2005 and 2004:

As of December 31, 2005 (in thousands):	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
Common stock in a public company	$ 28	$ 36	$ —	$ 64
Certificates of deposit	325	—	—	325
Corporate bonds	7,158	—	(6)	7,152
Government securities	2,500	1	(9)	2,492
Commercial paper	9,809	10	(3)	9,816
Asset-backed securities	4,863	—	(5)	4,858
Total	$24,683	$ 47	$ (23)	$24,707

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

Gross realized gains on sales of marketable securities in 2005 were $33,700. There were no realized gains or losses on the sales of marketable securities in 2004 or 2003.

NOTE 4—PROPERTY AND EQUIPMENT:

Property and equipment comprise the following (in thousands):

	December 31,	
	2005	2004
Computer and office equipment	$ 330	$ 73
Laboratory equipment	728	437
Leasehold improvements	1,426	1,401
	2,484	1,911
Less: Accumulated depreciation	(817)	(244)
	$1,667	$1,667

Depreciation expense was $573,000, $143,000, $90,000 and $817,000 for the years ended December 31, 2005, 2004 and 2003, and, cumulatively, for the period from October 17, 2001 (date of inception) to December 31, 2005, respectively.

Certain laboratory, computer and office equipment with a cost basis of approximately $0.7 million is collateral for borrowings under the loan and security agreement with Silicon Valley Bank.

NOTE 5—ACCRUED LIABILITIES:

Accrued liabilities comprise the following (in thousands):

	December 31,	
	2005	2004
Payroll and employee related expenses	$ 1,265	$ 449
Professional services	369	395
Other accrued expenses	524	218
	$ 2,158	$ 1,062

NOTE 6—NOTES PAYABLE:

On March 27, 2003, the Company entered into a loan and security agreement with Silicon Valley Bank to borrow up to $1.0 million for working capital and equipment purchases. The Company borrowed the full amount under this facility as of December 2004, which will be repaid over a 36-month period from the date of borrowing, at an average interest rate of 5.8% per annum. In connection with the agreement, the Company issued Silicon Valley Bank a warrant to purchase 38,000 shares of Series A redeemable convertible preferred stock, which was fully exercised in 2005.

At December 31, 2005, future principal payments under the loan and security agreement are as follows (in thousands):

Year Ending December 31,	
2006	$230
2007	151
Total	$381

Under the loan and security agreement, the Company is required to maintain the lower of 85% of its total cash and cash equivalents or $10.0 million with the financial institution. Borrowings under the equipment line of credit are collateralized by the related equipment. At December 31, 2005, the Company was in compliance with all covenants in the agreement.

NOTE 7—COMMITMENTS AND CONTINGENCIES:

On August 31, 2004, the Company entered into a noncancelable facility sublease agreement for 33,700 square feet of laboratory and office space. The lease was effective October 1, 2004 and expires February 2010. On April 1, 2005 the Company entered into a noncancelable facility operating lease for approximately 6,489 square feet of laboratory space, which expires in February 2010. In connection with the execution of the lease, the Company paid a security deposit of approximately $25,000. The future rental payments required by the Company under the noncancelable operating lease and sublease as of December 31, 2005 are as follows (in thousands):

Years Ended December 31,	
2006	$ 540
2007	560
2008	665
2009	686
2010	114
Future minimum rental payments	$ 2,565

Rent expense for the years ended December 31, 2005, 2004, 2003, and, cumulatively, for the period from October 17, 2001 (date of inception) to December 31, 2005 was $545,000, $726,000, $447,000, and $1,856,000, respectively.

The Company's purchase commitments at December 31, 2005 totaled $106,000.

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, 2005.

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, 2005.

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. Future aggregate milestone payments under this agreement could total €1.8 million (approximately $2.1 million based on the exchange rate at December 31, 2005).

In November 2004, the Company entered into an agreement with MediBIC Co. Ltd. (MediBIC) to develop glufosfamide in Japan and several other Asian countries, and received an upfront payment of $5.0 million contingent upon the finalization of the clinical development plan. In July 2005, the Company finalized the development plan with MediBIC and began recognizing revenue from the upfront payment on a straight-line basis over the development period, currently estimated to be through 2008. The Company is responsible for all development activities under this agreement. 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 million to $15 million, depending on the stage of development. The chief operating officer and director of a subsidiary of MediBIC, is the wife of the Company's chief executive officer.

The unamortized portion of the upfront payment has been classified as deferred revenue on the Company's consolidated balance sheet at December 31, 2005. The entire upfront payment was classified as "Advance on research and development contract" on the Company's consolidated balance sheet at December 31, 2004, reflecting the contingency that existed at that time.

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

All of the shares of redeemable convertible preferred stock were converted into 20,552,812 shares of common stock upon completion of the Company's initial public offering in February 2005.

As of December 31, 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	

Sale of Series B redeemable convertible preferred stock

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 loan and security agreement in March 2003, the Company issued a warrant to Silicon Valley Bank to purchase an aggregate of 38,000 shares of Series A redeemable convertible preferred stock at an exercise price of $1.00 per share. Upon the closing of the initial public offering in February 2005, this warrant was converted into a warrant to purchase 23,073 shares of common stock. The warrant was fully vested and exercisable upon grant, and was exercised in 2005. The fair value of the warrant was reflected as an other asset and was amortized to interest expense on a straight-line basis over the term of the loan and security agreement.

NOTE 9—STOCKHOLDERS' EQUITY (DEFICIT):

Common stock

On February 4, 2005, the Company completed its initial public offering of 6.1 million shares of common stock for net proceeds totaling $38.1 million. On October 14, 2005, the Company completed a public offering of 6.4 million shares of its common stock for net proceeds totaling $62.4 million. 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, 2005.

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. In August 2005, the founder resigned from the Company and entered into a consulting and stock vesting agreement. Under the terms of this agreement, the vesting of his restricted stock accelerated at December 31, 2005, and compensation expense associated with the accelerated vesting of these options was recorded for his services as a consultant through December 31, 2005. 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. The shares vest over a six-year period. The unvested shares of common stock are subject to repurchase by the Company in the event of termination of the consulting relationship. Included in common stock as of December 31, 2005, 2004 and 2003 for both awards are 4,849, 55,168 and 75,970 shares subject to the Company's right of repurchase, respectively.

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 consolidated financial statements were retroactively adjusted to reflect the stock split.

Equity Incentive Plans

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. In 2005, 2,428,805 shares of common stock were authorized for issuance pursuant to the 2004 Plan, plus any shares which had been reserved but not issued under the 2001 Equity Incentive Plan (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.

On December 20, 2005, the Board of Directors approved an additional 1,214,402 shares for issuance under the 2004 Plan effective January 1, 2006.

Activity under the 2001 Plan and 2004 Plan is set forth below:

	Shares Available for Grant	Outstanding Options		Weighted Average Exercise Price
		Number of Shares	Exercise Price	
Shares reserved at Plan inception	1,214,402	—	$ —	$ —
Balances, December 31, 2001	1,214,402	—	—	—
Options granted	(1,080,024)	1,080,024	0.16	0.16
Options exercised	—	(2,428)	0.16	0.16
Balances, December 31, 2002	134,378	1,077,596	0.16	0.16
Additional shares reserved	3,036,007	—	—	—
Options granted	(726,564)	726,564	0.16–0.26	0.16
Options exercised	—	(7,711)	0.16	0.16
Options canceled	5,568	(5,568)	0.16	0.16
Balances, December 31, 2003	2,449,389	1,790,881	0.16–0.26	0.16
Options granted	(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
Additional shares reserved	2,428,805	—		
Options granted	(947,187)	947,187	0.53–14.98	8.22
Options exercised	—	(453,317)	0.16–0.53	0.49
Options canceled	14,850	(14,850)	5.80–12.45	6.62
Options repurchased	63,969	—	0.16–0.53	0.41
Balances, December 31, 2005	1,835,066	926,357	0.16–14.98	8.29

At December 31, 2005 and 2004, stock options outstanding and vested by exercise price were as follows:

	December 31, 2005			December 31, 2004		
Exercise Price	Number of Options Outstanding	Number Vested	Weighted Average Remaining Contractual Life (Years)	Number of Options Outstanding	Number Vested	Weighted Average Remaining Contractual Life (Years)
$ 0.16	27,073	19,798	7.29	74,595	49,997	7.78
$ 0.26	23,720	8,348	8.19	26,946	4,743	9.19
$ 0.53	186,714	141,107	8.47	345,796	8,770	9.64
$ 5.80	600	—	9.20	—	—	—
$ 6.26	165,750	61,249	9.38	—	—	—
$ 6.49	28,500	—	9.39	—	—	—
$ 6.85	20,000	—	9.43	—	—	—
$12.45	353,500	—	9.70	—	—	—
$14.93	30,000	—	9.98			
$14.98	90,500	—	9.97	—	—	—
	926,357	230,502	9.31	447,337	63,510	9.30

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

Before the initial public offering in February 2005, the 2001 Plan allowed options to be exercised prior to vesting. Included in common stock at December 31, 2005 are 1,469,765 shares subject to repurchase related to options exercised prior to vesting.

Deferred stock-based compensation

There were no below-market grants subsequent to the initial public offering in February 2005. Prior to the initial public offering, 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, 2005, 2004 and 2003, the Company has recorded deferred stock-based compensation related to these options of approximately $0.5 million, $14.4 million and $2.3 million, net of cancellations, respectively.

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,		
	2005	2004	2003
Research and development	$ 2,061	$ 2,279	$ 57
General and administrative	3,263	3,015	753
	$ 5,324	$ 5,294	$ 810

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. 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. 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 $6.0 million and stock compensation expense of $2.4 million during the year ended December 31, 2004. Beginning in 2005, the remaining deferred stock-based compensation related to these options is being amortized on a straight-line basis over the remaining option vesting period.

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, 2005, 2004 and 2003, 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,		
	2005	2004	2003
Risk-free interest rate	4.25%	4.38%	4.26%
Expected life (in years)	10	10	10
Dividend yield	—	—	—
Expected volatility	80%	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 $4.1 million, $681,000 and $256,000 for the years ended December 31, 2005, 2004 and 2003, respectively. In August 2005, the president and founder of the Company resigned as president and entered into a consulting and stock vesting agreement. Under the terms of this agreement, the vesting of certain of his options accelerated at December 31, 2005, subject to certain conditions. Due to the change in status from that of an employee to a consultant, compensation expense associated with the accelerated vesting of these options was recorded for his services as a consultant through December 31, 2005. Stock-based compensation expenses related to options granted to non-employees were entirely expensed to research and development.

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. For the year ended December 31, 2005, employees had purchased 58,522 shares of common stock under the Purchase Plan at an average price of $5.95 per share. At December 31, 2005, plan participants had $246,000 withheld to purchase stock on February 15, 2006, which is included in accrued liabilities on the accompanying balance sheet.

Directors Compensation Program

On December 20, 2005, the Board of Directors approved revised compensation arrangements for non-employee directors of the Company. Effective January 1, 2006, non-employee directors receive an annual retainer $30,000, and, in addition, chairpersons of the Audit, Compensation and Nominating and Corporate Governance Committees receive annual retainers of $16,000, $14,000, and $10,000, respectively. On May 19, 2005, each non-employee director was granted an option to purchase 15,000 shares of the Company's common stock under the Company's 2004 Equity Incentive Plan. In addition, at each annual meeting of stockholders of the Company, each non-employee director who has served as director at least six months prior to such meeting will receive an automatic grant of an option to purchase 15,000 shares of the Company's common stock.

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):

	2005	2004	2003
U.S. federal taxes (benefit) at statutory rate	$(15,099)	$(8,013)	$(2,823)
State federal income tax benefit	(2,428)	(1,374)	—
Unutilized (utilized) net operating losses	16,944	6,075	2,539
Stock-based compensation	200	1,919	276
Research and development credits	(738)	(554)	—
Tax assets not benefited	1,112	1,947	8
Other	9	—	—
Total	$ —	$ —	$ —

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,		
	2005	2004	2003
Capitalized start-up costs	$ 408	$ 1,014	$ 605
Net operating loss carryforwards	24,043	9,482	3,407
Research and development credits	2,112	874	385
Other (stock-based compensation, accruals, reserves, depreciation)	4,503	852	49
Total deferred tax assets	31,066	12,222	4,446
Less: Valuation allowance	(31,066)	(12,222)	(4,446)
	$ —	$ —	$ —

At December 31, 2005, the Company had federal and state net operating loss carryforwards of approximately $61.0 million available to offset future taxable income. The Company's federal and state net operating loss carryforwards will begin to expire in 2021 and 2013, 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, 2005, the Company had federal research and development tax credits of approximately $1.3 million, which will expire in years 2021 through 2025, and state research and development tax credits of approximately $1.2 million, which will have no expiration date.

The Company has established a valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

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, 2005, the Company has not made any contributions to the 401(k) Plan.

NOTE 12—SUBSEQUENT EVENTS:

On February 3, 2006, the Company, entered into a lease under which it will lease an additional 34,205 square feet of space and increase the lease term for the existing 34,205 square feet of space located at the Company's headquarters in Redwood City, California. The lease is for a period of 66 months, and will begin on April 1, 2006 with respect to the additional square footage and on March 1, 2010 with respect to the existing square footage. The lease will expire, unless otherwise terminated under the terms of the lease, on September 30, 2011. The aggregate rent for the term of the lease is approximately $4.8 million. In addition, the lease requires the Company to pay certain taxes, assessments, fees and other costs and expenses associated with the premises in amounts yet to be determined as well as a customary management fee. The Company will also be responsible for the costs of certain tenant improvements associated with the leased space. In connection with the lease, the Company will furnish a letter of credit in customary form to the landlord in an amount of approximately $0.3 million.

NOTE 13—QUARTERLY FINANCIAL DATA (UNAUDITED):

The following table presents certain unaudited quarterly financial information for the eight quarters ended December 31, 2005. This information has been prepared on the same basis as the audited consolidated financial statements and includes all adjustments necessary to present fairly the unaudited quarterly results of operations.

2005	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share data)				
Net loss attributable to common stockholders	$ (7,540)	$ (10,186)	$ (11,526)	$ (15,156)
Basic and diluted net loss per share attributable to common stockholders	$ (0.46)	$ (0.36)	$ (0.40)	$ (0.44)
Shares used in computation of basic and diluted net loss per share	16,340	28,679	28,961	34,452
2004				
(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

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, 2005, 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.

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.

ITEM 9B. OTHER INFORMATION

None.

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, 2005 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, 2005 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, 2005 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, 2005 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, 2005 and is hereby incorporated by reference.

PART IV

ITEM 15. EXHIBITSAND FINANCIAL 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:

(2) All financial statement supporting schedules are omitted because the information is inapplicable or presented in the Notes to Consolidated 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 Registrant
4.1(3)	Specimen Certificate evidencing shares of common stock
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
10.3(3)+	2004 Employee Stock Purchase Plan
10.4(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†	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
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

EXHIBIT NUMBER	DESCRIPTION
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 B. Colowick
10.18(3)	Letter Agreement amending Development Agreement by and between the Registrant and MediBIC Co. Ltd.
10.19(4)+	Employment Letter Agreement by and between the Registrant and Alan B. Colowick dated October 25, 2004
10.20(5)+	Amended and Restated 2004 Equity Incentive Plan
10.21(6)+	Consulting Agreement and Amendment to Stock Vesting Agreement by and between the Registrant and Dr. George F. Tidmarsh dated August 18, 2005
10.22(7)+	Offer Letter by and between the Registrant and Michael S. Ostrach dated as of September 2, 2005
10.23(7)+	Form of Change of Control Severance Agreement by and between the Registrant and executive officers other than those covered by Exhibit 10.15
10.24(8)	Triple Net Space Lease by and between the Registrant and Pacific Shores Investors, LLC, sated January 31, 2006
10.25(9)	Form of Notice of Grant of Stock Options and Stock Option Agreement
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
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 exhibit to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004, and incorporated herein by reference.

(4) Filed as the like number exhibit to our Quarterly Report on Form 10-Q filed on May 13, 2005, and incorporated herein by reference.

(5) Filed as the like number exhibit to our Current Report on Form 8-K filed on May 24, 2005, and incorporated herein by reference.

(6) Filed as exhibit 10.20 to our Current Report on Form 8-K filed on August 19, 2005, and incorporated herein by reference.

(7) Filed as the like number exhibit to our Current Report on Form 8-K filed on September 16, 2005, and incorporated herein by reference.

(8) Filed as exhibit 10.24 to our Current Report on Form 8-K filed on February 9, 2006, and incorporated herein by reference.

(9) Filed as exhibit 10.25 to our Current Report on Form 8-K filed on March 17, 2006, 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.

+ Indicates a management contract or compensatory plan or arrangement.

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 28, 2006

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 28, 2006
/s/ JANET I. SWEARSON **Janet I. Swearson**	Chief Financial Officer (principal financial and accounting officer)	March 28, 2006
/s/ BRUCE C. COZADD **Bruce C. Cozadd**	Director	March 28, 2006
/s/ PATRICK G. ENRIGHT **Patrick G. Enright**	Director	March 28, 2006
/s/ WILLIAM A. HALTER **William A. Halter**	Director	March 28, 2006
/s/ WILFRED E. JAEGER, M.D. **Wilfred E. Jaeger, M.D.**	Director	March 28, 2006
/s/ GEORGE G. C. PARKER, PH.D. **George G. C. Parker, Ph.D.**	Director	March 28, 2006
/s/ MICHAEL F. POWELL, PH.D. **Michael F. Powell, Ph.D.**	Director	March 28, 2006
/s/ GEORGE F. TIDMARSH, M.D., PH.D. **George F. Tidmarsh, M.D., Ph.D.**	Director	March 28, 2006

EXHIBIT 10.10

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

Agreement

between

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

and

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

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

Whereas

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

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

1. Subject

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

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

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

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

in respect of THL3; and

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

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

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

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

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

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

A grant to Acraf, and Acraf does hereby accept:

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

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

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

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

Parties agree that:

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

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

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

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

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

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

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

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

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

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

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

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

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

1.7 TH undertakes to report to Acraf:

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

obtained;

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

2. Development Plan

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

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

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

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

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

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

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

3. Active Ingredient

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

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

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

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

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

4. Duration

4.1 Parties agree that:

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

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

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

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

5. Results and Intellectual Property Rights

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

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

6. Confidentiality

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

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

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

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

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

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

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

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

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

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

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

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

7. Amendment

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

8. Good Faith

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

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

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

supranational treaties, laws, rules and regulations applicable hereto.

9. Force Majeure

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

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

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

10. Communication

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

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

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

11. Applicable Law and Jurisdiction

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

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

12. Relationship of the Parties

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

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

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

13. Further Assurances

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

14. Entire Agreement, Waiver, Amendment.

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

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

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

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

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

15. Other provisions

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

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

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

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

Annex **A**
Development Plan

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

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

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

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

Annex **B**
TH Territory

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

Annex **C**
Acraf Territory

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

EEA Members
Iceland,
Liechtenstein,
Norway

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

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-126276) of Threshold Pharmaceuticals, Inc. of our report dated March 27, 2006 relating to the financial statements, which appear in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

San Jose, California
March 28, 2006

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 officer 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 28, 2006

/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 officer 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 28, 2006

/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, 2005, 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 28, 2006

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

The foregoing certification is being furnished pursuant to 18 U.S.C. Section 1350. It is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and it is not being incorporated by reference into any filing of the Company, regardless of any general incorporation language in such filing.

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, 2005, 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 28, 2006

/s/ Janet I. Swearson

Janet I. Swearson
Chief Financial Officer

The foregoing certification is being furnished pursuant to 18 U.S.C. Section 1350. It is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and it is not being incorporated by reference into any filing of the Company, regardless of any general incorporation language in such filing.