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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, 2012

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: 001-32979

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)**
170 Harbor Way, Suite 300, South San Francisco, CA 94080	**94080**
(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:

Title of Each Class	**Name of Each Exchange On Which Registered**
Common Stock $0.001 Par Value	**NASDAQ Capital Market**
Series A Participating Preferred Stock	**NASDAQ Capital Market**

Securities registered pursuant to Section 12(g) of the act: None

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 whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐	Accelerated filer ☒	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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 Capital Market on June 30, 2012 was approximately $342,842,599.

On February 28, 2013 there were 56,535,805 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 17, 2013, or the Proxy Statement, are incorporated herein by reference into Part III.

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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 (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). We may, in some cases, use words such as "project," "believe," "anticipate," "plan," "expect," "estimate," "intend," "should," "would," "could," "potentially," "possible", "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, conduct and complete, and the timing of the commencement, conduct and completion of clinical trials for TH-302 and any additional compounds we develop;
- our financial condition and potential milestone payments we may receive under our license and co-development agreement with Merck KGaA;
- the success of any clinical trials that we commence;
- the timing of results of our clinical trials;
- our receipt and the timing of regulatory approvals, and our satisfaction of ongoing regulatory review;
- our ability to establish and maintain intellectual property rights in our product candidates;
- our ability to timely develop a formulation of TH-302 that will be suitable for commercial production;
- whether any product candidates that we are able to commercialize are safer or more effective than other marketed products, treatments or therapies;
- the ability of our licensee of glufosfamide to develop, manufacture, market and otherwise commercialize glufosfamide, and to raise sufficient funds to commence clinical development;
- our research and development activities, including development of new product candidates, and projected expenditures;
- our ability to complete preclinical and clinical testing successfully 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 ability to raise capital when needed; 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," the "Company," "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

We are a biotechnology company using our expertise in the tumor microenvironment to discover and develop therapeutic agents that selectively target tumor cells for the treatment of patients living with cancer. Our lead investigational small molecule, TH-302, is being evaluated in two pivotal Phase 3 clinical trials and multiple earlier-stage clinical trials. We have a global license and co-development agreement for TH-302 with Merck KGaA, with an option to co-commercialize in the United States.

TH-302 was discovered by our scientists based on our hypoxia-activated prodrug ("HAP") technology. Hypoxia, or abnormally low oxygen concentration, is a common feature of the tumor microenvironment in most solid tumors and in the bone marrow of patients with some hematological malignancies (also known as blood cancers, for example, leukemias and multiple myeloma). Tumor hypoxia is associated with the development of resistance to traditional anticancer treatments, including chemotherapy and radiotherapy, enhanced metastatic potential, and ultimately treatment failure. Normal healthy tissues, in contrast, are well oxygenated and typically are not hypoxic. As a prodrug, TH-302 is designed to remain essentially inactive in normal tissues, but to activate under conditions of tumor hypoxia. Upon activation, TH-302 releases bromo isophosphoramide mustard (Br-IPM), a potent cytotoxin that kills cells by causing DNA to crosslink.

We believe that by virtue of targeting tumor hypoxia, TH-302 has broad clinical applicability across many types of solid tumors and some hematological malignancies. To explore this broad therapeutic potential of TH-302, we are conducting multiple clinical trials to evaluate its safety and efficacy as monotherapy and in combination with currently marketed anticancer drugs, including traditional chemotherapeutic agents and antiangiogenic agents.

We along with our partner Merck KGaA, under its division Merck Serono, are investigating TH-302 in the following clinical studies, which are actively recruiting patients:

Clinical Trial	Sponsor	Therapeutic Area	Combination therapy with TH-302	Clinical Status
TH-CR-406	Threshold	Soft Tissue Sarcoma	doxorubicin	Pivotal Phase 3
MAESTRO	Merck Serono	Pancreatic Cancer	gemcitabine	Pivotal Phase 3
TH-CR-407	Threshold	Advanced Leukemias	None (TH-302 monotherapy)	Phase 1
TH-CR-408	Threshold	Multiple Myeloma	dexamethasone with or without bortezomib	Phase 1/2
TH-CR-410	Threshold	RCC, GIST, PNET	sunitinib	Phase 1

RCC=renal cell carcinoma; GIST=gastrointestinal stromal tumors; PNET=pancreatic neuroendocrine tumors

In addition, TH-302 is the subject of the following Investigator Sponsored Trials, which are actively recruiting patients:

Study Sponsor	Therapeutic Area	Combination Therapy with TH-302	Clinical Status
The University of Texas Health Science Center at San Antonio	Astrocytoma	bevacizumab	Phase 1/2
Duke University Medical Center	Various Solid Tumors	pazopanib	Phase 1
North Central Cancer Treatment Group	Advanced Kidney Cancer or Liver Cancer	sorafenib	Phase 1

Our Strategy

We are focused on building a fully integrated biopharmaceutical company that discovers, develops, and commercializes drugs for cancer based on targeting the tumor microenvironment. We focus on prodrugs of known chemotherapeutic agents or related analogs that undergo relatively selective activation in the tumor microenvironment and potentially allow for an improved safety and efficacy profile for the drug. Key elements of our strategy are to:

- ***Develop TH-302 successfully.*** We believe that by virtue of targeting tumor hypoxia—a common feature of solid tumors and some hematological malignancies—TH-302 may have broad clinical applicability across many types of solid tumors and blood cancers. To maximize the value of TH-302, we are conducting clinical trials in therapeutic areas where preclinical and clinical data are supportive of TH-302's activity. We are focused on successful execution of clinical and regulatory strategies to support submissions for regulatory approval of TH-302 in the most expedient manner. We will continue to work on broadening the applicability of TH-302 to other cancers and in combination with other approved anticancer drugs.
- ***Continue to broaden our pipeline by 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 will continue to investigate drug candidates from our hypoxia activated prodrug platform for further development. We also may evaluate additional in-licensing opportunities that build on our expertise and complement our current pipeline.
- ***Build on our expertise in targeting the tumor microenvironment.*** We intend to continue our focused approach in research and clinical development. We believe our expertise in this area 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.

Tumor Hypoxia

Tumor hypoxia, or low oxygen concentration, is a result of disordered vasculature found in all solid tumors. Whereas normal healthy tissues are typically well oxygenated by virtue of having highly regular and structured arrays of blood vessels, the vasculature supporting cancerous tissues is highly disordered and irregular. Common abnormalities in tumor vasculature include a large variation in the distance between the blood vessels that carry oxygen and other vital nutrients as well as "dead-ends" and temporary occlusions. Furthermore, in tumors, the growth of malignant cells is unregulated resulting in these tissues literally outgrowing their blood supply, leading to severe deficiencies in the perfusion of oxygen and nutrients.

Together, abnormalities in tumor vasculature and the unregulated growth of cancer cells lead to distinctive hypoxic microenvironments not found in most normal tissues. Many traditional anticancer agents are not able to penetrate these hypoxic zones. Furthermore, cells that reside within regions of tumor hypoxia are relatively quiescent in contrast to highly proliferative cells that are the hallmark of cancer. As many traditional cancer therapies work by blocking cell division, they are not effective in killing the non-dividing, quiescent cells within hypoxic zones. Furthermore, cells subjected to prolonged hypoxia are thought to accumulate the changes in their growth properties and genetic mutations that can lead to drug resistance, enhanced metastatic potential, and, ultimately, treatment failure.

Given its central role in tumor progression, metastasis, resistance, and ultimately treatment failure, hypoxia is emerging as a significant, high-priority target for cancer therapy.

TH-302 Investigational Hypoxia-targeted Drug

The introduction of therapies that selectively target tumor hypoxia offers the potential to selectively target tumors and expand the therapeutic options available for cancer patients across the majority of tumor types. To

our knowledge, TH-302 is the most clinically advanced hypoxia-targeted drug in active development for the treatment of cancer. TH-302 is designed as a prodrug that is selectively activated under the extreme hypoxic conditions commonly found in tumors, but not typically in healthy tissues. Within regions of tumor hypoxia, TH-302 is converted to its active form, bromo isophosphoramide mustard (Br-IPM). Variants of IPM are clinically validated potent DNA alkylating agents, which kill tumor cells by causing DNA to crosslink thereby rendering cells unable to replicate their DNA and divide. Once activated in hypoxic tissues, Br-IPM can also diffuse into surrounding oxygenated regions of the tumor and kill cells there via a "bystander effect".

Preclinical and clinical data suggest that TH-302 has significant antitumor activity both alone as well as in combination with other cancer therapies that target the rapidly proliferating cells found in normally oxygenated regions of solid tumors. Because of its preferential activation in the hypoxic regions of solid tumors, we believe that TH-302 will be less likely to produce the systemic toxicity caused by untargeted cytotoxic chemotherapies. Preclinical studies have also shown enhanced antitumor activity of TH-302 when combined with antiangiogenic agents, which are drugs designed to disrupt the blood vessel network supplying tumors. The underlying biological rationale for this enhanced activity is based, in part, on evidence that antiangiogenic agents increase levels of tumor hypoxia. Other research suggests that the bone marrow of patients with leukemia as well as multiple myeloma is also highly hypoxic and supports the potential therapeutic utility of TH-302 in treating these blood cancers.

TH-302 Clinical Development Programs

The development plan for TH-302 is designed to investigate its safety and efficacy across a broad range of solid tumors and hematologic malignancies. We are developing TH-302 in areas supported by preclinical and clinical data and where there is high unmet need for new anticancer agents. To date, TH-302 has been evaluated in more than 750 patients with cancer.

We completed a monotherapy Phase 1 clinical trial that determined the maximum tolerated dose, dose limiting toxicities, safety, pharmacokinetics and preliminary efficacy of TH-302 monotherapy in patients with advanced solid tumors. We expanded enrollment in this trial to investigate TH-302 as a single agent in specific indications in which monotherapy activity had been observed as well as in some indications in which notable activity had been documented in combination with other chemotherapy drugs. We completed enrollment in two combination therapy Phase 1/2 clinical trials that determined the maximum tolerated doses, dose-limiting toxicities, safety, pharmacokinetics and preliminary efficacy of TH-302 in combination with four currently approved chemotherapies. Data from this collection of clinical trials supported our initial randomized controlled trial of TH-302 in first-line pancreatic cancer.

The most advanced clinical trials of TH-302 are two pivotal Phase 3 trials: one in combination with doxorubicin versus doxorubicin alone in patients with soft tissue sarcoma, and the other in combination with gemcitabine versus gemcitabine plus placebo in patients with advanced pancreatic cancer. Both Phase 3 trials are being conducted under Special Protocol Assessments with the U.S. Food and Drug Administration (FDA). The FDA and the European Commission have granted TH-302 Orphan Drug Designation for the treatment of soft tissue sarcoma. Initiation of these studies was supported by preclinical data in disease-specific models as well as data from Phase 2 trials in the same patient populations.

We are also conducting Phase 1/2 clinical trials of TH-302 in patients with advanced leukemias and multiple myeloma based on research demonstrating that hypoxia in the bone marrow is characteristic of some hematological malignancies. Likewise, research has demonstrated that treatment with antiangiogenic agents can increase tumor hypoxia, providing the underlying rationale for current investigations of TH-302 in combination with four marketed antiangiogenic agents in four different Phase 1/2 clinical trials.

We continue to evaluate and intend to pursue additional therapeutic areas, development pathways and regulatory strategies to optimize the potential therapeutic applications of, and market opportunities for, TH-302.

TH-302 pivotal Phase 3 program in soft tissue sarcoma:TH-302 in combination with doxorubicin

In partnership with the Sarcoma Alliance for Research through Collaboration (SARC), we are conducting the 406 trial. This is an international, randomized, pivotal Phase 3 trial designed to enroll 450 patients with metastatic or locally advanced unresectable soft tissue sarcoma (STS) who have not previously received chemotherapy. The trial is designed to evaluate the efficacy and safety of TH-302 in combination with doxorubicin, compared to doxorubicin alone. The study is under a Special Protocol Assessment agreement with the U.S. FDA; overall survival is the primary efficacy endpoint; additional endpoints include efficacy measured by progression-free survival, overall response rate, overall survival at 6 and 12 months, progression free rate at 3 months and progression-free rate at 6 months, duration of response, stable disease or better rate, change in ECOG and performance status, as well as assessments of safety and tolerability, pharmacokinetics and biomarkers. The FDA and the European Commission have granted TH-302 Orphan Drug Designation for the treatment of STS.

This Phase 3 trial for TH-302 was initiated following results from a multi-center, dose-escalation Phase 1/2 trial of TH-302 in patients with STS (the 403 trial). The 403 trial was designed to determine the safety, efficacy and pharmacokinetics of TH-302 in combination with full-dose doxorubicin in patients with STS followed by TH-302 maintenance monotherapy for patients who had not progressed after six cycles of combination therapy. Dose-limiting toxicities at a TH-302 dose of 340 mg/m^2 were Grade 4 thrombocytopenia and Grade 3 infection with Grade 4 neutropenia. The maximum tolerated dose (MTD) of 300 mg/m^2 was established for TH-302 in combination with the approved dose of 75 mg/m^2 doxorubicin with prophylactic growth factor support. Enrollment was expanded at the MTD, and a total of 91 patients with advanced STS previously untreated with systemic chemotherapy were enrolled and treated at the MTD.

At the 2012 annual meeting of the Connective Tissue Oncology Society, updated data from the Phase 2 portion of the 403 trial were presented including median progression free survival of 6.7 months (95% CI: 6.2 to 8.1 months); median overall survival of 21.5 months (95% CI 16.0 to 27.6 months); one-year survival of 73% (95% CI: 63% to 82%); two-year survival of 44% (95% CI: 32% to 55%), and; overall best response (partial and complete responses, unconfirmed) of 36%.

Development Activities Planned for 2013: We continue to enroll patients in the Phase 3 trial and currently expect to complete enrollment around the end of 2013.

TH-302 pivotal Phase 3 program in pancreatic cancer: TH-302 in combination with gemcitabine

In December 2012, our partner Merck KGaA, through its division Merck Serono, opened the global Phase 3 MAESTRO study assessing the efficacy and safety of TH-302 in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma. MAESTRO stands for TH-302 in the treatment of **M**etast**A**tic or unr**ES**ectable pancrea**T**ic adenoca**R**cin**O**ma.

MAESTRO is a randomized, placebo-controlled, international, multi-center, double-blind Phase 3 trial of TH-302 plus gemcitabine compared with placebo plus gemcitabine and is expected to enroll 660 patients. The primary efficacy endpoint is overall survival; the secondary endpoints include efficacy measured by progression-free survival (PFS), overall response rate and disease control rate, as well as assessments of safety and tolerability, pharmacokinetics and biomarkers. The study is being conducted under a Special Protocol Assessment (SPA) agreement with the U.S. FDA.

The Phase 3 trial for TH-302 was initiated following results from a randomized, controlled Phase 2b trial of TH-302 in combination with gemcitabine in patients with first-line pancreatic cancer (404 trial). A total of 214 patients with previously untreated, locally advanced, unresectable or metastatic pancreatic adenocarcinoma were enrolled and treated in the clinical trial at 45 sites in the United States. Patients were randomized equally into one of three cohorts: TH-302 at a dose of 240 mg/m2 plus gemcitabine or TH-302 at a dose of 340 mg/m2 plus gemcitabine or gemcitabine alone. If a patient's cancer progressed while on gemcitabine alone, the patient could

crossover and be randomized into one of the TH-302 plus gemcitabine cohorts. The primary efficacy endpoint of the trial was a comparison of progression free survival between the two pooled combination arms and the gemcitabine alone arm. The secondary endpoints were overall response rate, overall survival, event-free survival, CA 19-9 response rate as well as various safety parameters.

In February of 2012 we reported top-line results from the randomized and controlled Phase 2 trial of TH-302 plus gemcitabine in patients with pancreatic cancer (404 trial). The median progression-free survival was 5.6 months for patients treated with gemcitabine in combination with TH-302 at 240 mg/m2 and 340 mg/m2 compared to 3.6 months for patients treated with gemcitabine alone. The progression free survival hazard ratio comparing the TH-302 combinations to gemcitabine alone was 0.61 (95% confidence interval: 0.43-0.87) which was highly statistically significant (p = 0.005) and represented a 63% improvement in progression free survival. The response rate in the combination arms was 22% compared to 12% in the gemcitabine alone group. Results also demonstrated greater efficacy in the higher TH-302 dose group compared to the lower dose group. The combination had a safety profile that was consistent with our prior study of this combination regimen. As in that study, skin and mucosal toxicities related to TH-302 were dose dependent but not dose limiting. In April 2012, we provided detailed results from our 404 trial at the American Association of Cancer Research (AACR) annual meeting including results for each of the 240 mg/m2 and 340 mg/m2 TH-302 combination arms. The median progression free survival was 6.0 months in the 340 mg/m2 group. The response rate was 27% in the 340 mg/m2 group. A similar dose dependency was reported in serum CA19-9 levels. There was greater drug exposure in the combination groups with a median of 4 cycles received with gemcitabine alone compared with 5 cycles in the 240 mg/m2 group and 6 cycles in the 340 mg/m2 group. The combination safety profile was consistent with the prior study of this combination regimen. As in that study, skin and mucosal toxicities were less than what had been seen at the single-agent maximum tolerated dose of TH-302, which was previously established at 575 mg/m2. The incidence of Grade 3/4 thrombocytopenia and Grade 3/4 neutropenia was significantly higher in the combination arms and highest in the 340 mg/m2 group. Discontinuations for adverse events were lowest, however in the 340 mg/m2 group.

In September 2012, at the European Society for Medical Oncology (ESMO) 2012 Congress, updated results were presented confirming a significant improvement (p=0.008) in progression free survival. The updated progression free survival hazard ratio comparing the TH-302 combinations to gemcitabine alone was 0.64 (95% confidence interval: 0.45 – 0.89). This was associated with a 2.4-month increase in median progression free survival for patients receiving TH-302 340 mg/m^2. New findings from the Phase 2b trial were presented including an analysis of overall survival, which was a secondary endpoint of the study. This analysis indicated that patients treated with gemcitabine alone had a median overall survival of 6.9 months compared with 9.2 months for patients treated with 340 mg/m2 TH-302 plus gemcitabine (HR: 0.955, 95% CI: 0.67-1.37, p=0.800) and 8.7 months for patients treated with 240 mg/m2 TH-302 plus gemcitabine (HR: 0.960, 95% CI: 0.67-1.38, p=0.827). While not statistically significant, the improvement in median overall survival is consistent with the improvement in median progression free survival reported previously. The trial was not designed to detect a statistically significant improvement in overall survival and included a cross-over component. Patients receiving gemcitabine alone who crossed over to receive gemcitabine plus TH-302 upon disease progression contributed to an increase in survival of the control arm. TH-302 continued to demonstrate a safety profile consistent with what had been previously reported at AACR. The most common adverse events were fatigue, nausea, constipation and peripheral edema, and were similar across groups. Skin and mucosal toxicities and myelosuppression were the most common adverse events related to TH-302, were mostly Grade 1 and 2, and did not result in increases in treatment discontinuation. Adverse events leading to discontinuation of study treatment as well as serious adverse events were balanced across all treatment arms. Grade 3/4/5 adverse events were generally below 10%.

Development activities planned for 2013: Merck Serono is responsible for conduct and execution of the MAESTRO Phase 3 study and enrollment in the study is ongoing.

TH-302 program in hematological malignancies: leukemia and multiple myeloma

The role of hypoxia in the pathogenesis of hematological malignancies (also known as blood cancers, for example, leukemias and multiple myeloma) and its role in disease progression is an emerging area of active research in the cancer biology community. Preclinical studies have been conducted to investigate TH-302 in models of multiple myeloma. I*n vitro* studies demonstrated that TH-302 induces apoptosis (programmed cell death) and has strong synergistic cytotoxic effect in combination with bortezomib, a proteasome inhibitor indicated for the treatment of patients with multiple myeloma. In *in vivo* models of multiple myeloma, the combination of TH-302 plus bortezomib was associated with statistically significant improvements in multiple disease parameters including a reduction in circulating paraprotein levels, the standard endpoint for assessing drug efficacy in multiple myeloma. Preclinical studies have also investigated TH-302 in models of leukemia. TH-302 treatment resulted in marked *in vitro* hypoxic-specific cell death of human leukemia cells under the same conditions where traditional chemotherapeutic agents such as cytarabine and doxorubicin were not effective. *In vivo*, TH-302 treatment significantly inhibited leukemia disease progression in a preclinical model of human leukemia. These studies in hematological malignancy models provide the basis for the ongoing clinical trials of TH-302 in patients with multiple myeloma and leukemia.

TH-CR-407 Phase 1 Trial in Patients with Advanced Leukemias

In June 2010, we initiated a Phase 1 open label clinical trial of TH-302 designed to determine the maximum tolerated dose, dose limiting toxicity, safety, tolerability, clinical activity, and pharmacokinetics of TH-302 in patients with advanced leukemia (the TH-CR-407 trial). The starting dose of TH-302 was 120 mg/m2 administered daily for 5 days of a 21-day cycle. At the highest dose investigated in this study (550 mg/m2), two patients developed dose limiting mucosal toxicity. The maximum tolerated daily dose of TH-302 was established at 460 mg/m2. Although Phase 1 trials are not designed to assess efficacy, we have noted that in this trial, TH-302 appears to be active, as evidenced by stabilization or reduction of bone marrow and peripheral blast counts. One patient had a complete response and another patient had a complete response with incomplete platelet recovery with resolution of leukemia cutis. These results are not statistically significant, and there can be no assurance that our initial results will be replicated with the treatment of additional patients.

Development Activities Planned for 2013: The 407 trial is ongoing at MD Anderson Cancer Center, Houston, Texas, and continues to enroll patients with the objective of evaluating a second dosing regimen of TH-302 in which TH-302 is administered as a continuous infusion over a 5-day period. Updated results are anticipated by the end of 2013.

TH-CR-408 Phase 1/2 Trial in Patients with Multiple Myeloma

In March 2012, we initiated a Phase 1/2 open label clinical trial of TH-302 to determine the maximum tolerated dose, dose limiting toxicity, safety, tolerability, clinical activity, and pharmacokinetics of TH-302 in patients with relapsed/refractory multiple myeloma. The objectives of the trial are to determine the maximum tolerated dose, dose-limiting toxicity, safety, tolerability, clinical activity and pharmacokinetics of TH-302 in patients with multiple myeloma. The study has three parts. The first part is designed to establish the maximum tolerated dose of TH-302 in combination with dexamethasone. This dose of TH-302 will be further evaluated in combination with dexamethasone in additional patients in the second part of the study. Lastly, the combination of TH-302 and dexamethasone with bortezomib will be investigated. Bortezomib, a proteasome inhibitor, is currently used to treat patients with multiple myeloma. This study is ongoing at Dana-Farber Cancer Institute.

Development Activities Planned for 2013: We expect to complete enrollment in Part 1 of the study and report preliminary results later in 2013.

TH-302 program with antiangiogenics

Antiangiogenics are a relatively new class of anticancer therapies that target the tumor vasculature. A goal of antiangiogenic therapy is to “starve” tumors by disrupting the blood vessel network supplying tumors with

oxygen and nutrients needed for survival and growth. Emerging preclinical research suggests that antiangiogenics may also induce tumor hypoxia. As TH-302 is designed to be selectively activated under conditions of severe tumor hypoxia, the combination of TH-302 with antiangiogenic therapy has the potential to be an effective anticancer treatment. Preclinical models demonstrated enhanced antitumor activity of TH-302 when used in combination with antiangiogenic therapies (sunitinib and sorafenib), which was directly related to the amount of hypoxia induced by different doses of these antiangiogenics.

Based on preclinical studies, we are actively exploring the potential of combining TH-302 with antiangiogenic therapies in a variety of tumor types in human clinical trials. Current studies include the following:

- TH-CR-410: A Phase 1 dose-escalation clinical trial evaluating the safety of TH-302 in combination with sunitinib in patients with advanced renal cell carcinoma (RCC), gastrointestinal stromal tumors (GIST), and pancreatic neuroendocrine tumors (PNET).
- A Phase 1/2 safety and efficacy study of TH-302 in patients with recurrent high grade astrocytoma following bevacizumab.
- A Phase 1 dose-escalation study of pazopanib in combination with TH-302 in patients with advanced solid tumors.
- A Phase 1/2 study of sorafenib in combination with TH-302: Phase 1 in patients with advanced renal cell carcinoma (RCC) and patients with advanced hepatocellular carcinoma (HCC) and Phase 2 in 1st line advanced HCC.

In November 2012, preliminary results from the Phase 2 study in patients with high grade astrocytoma were reported at the ESMO 2012 Congress. The study enrolls patients with recurrent glioblastoma whose disease has progressed following initial treatment with chemoradiotherapy and whose disease has then progressed following treatment with bevacizumab and who are scheduled for debulking craniotomy (brain surgery to remove tumor tissue). Patients are randomized to treatment with a single dose of TH-302 (575 mg/m2) or placebo prior to surgery, followed by postoperative combination therapy of bevacizumab (10 mg/m2 every two weeks) and TH-302 every 2 weeks (4 week cycle) until disease progression. No dose limiting toxicity was reported for the first two dose cohorts. There were no Grade 3 or 4 adverse events observed with 240 mg/m2 TH-302. One Grade 3 adverse event (skin ulceration) and no Grade 4 adverse events have been observed in the second cohort at 340 mg/m2 TH-302. Data from the first six patients treated with TH-302 plus bevacizumab in the first two dose cohorts were presented at the ESMO 2012 Congress. Examination of surgical specimens revealed extensive areas of hypoxia. Five patients had stable disease including one patient with a target lesion best response by Response Assessment in Neuro-Oncology (RANO) criteria. One patient had progressive disease.

Development Activities Planned for 2013: All four studies continue to enroll patients. We expect to present preliminary results from the combinations of TH-302 with antiangiogenic agents by the end of 2013.

Market Opportunities

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. Such cells are found in regions of the tumor that have an adequate blood supply and therefore receive nutrients and oxygen essential for cell division and growth. However, the vasculature supporting tumors is highly disorganized and irregular. This results in regions of the tumor that do not receive adequate amounts of nutrients and oxygen. Low oxygen concentration within a tumor is called “tumor hypoxia”. Traditional anticancer agents fail to address tumor hypoxia.

Many traditional anticancer agents are not able to penetrate into the hypoxic zones of tumors. Furthermore, cells that reside within regions of tumor hypoxia are relatively quiescent (dormant) in contrast to highly

proliferative cells that are the hallmark of cancer. As many traditional cancer therapies work by blocking cell division, they are not effective in killing the non-dividing, quiescent cells within hypoxic zones. It has also been demonstrated that cells subjected to prolonged hypoxia accumulate changes in their growth properties and genetic mutations that can lead to drug resistance, enhanced metastatic potential, and, ultimately, treatment failure.

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 which may lead to bleeding, infection and anemia, as well as other side effects, such as diarrhea and hair loss. Likewise, radiation generally cannot be administered without causing significant damage to healthy tissue surrounding a tumor.

Given its role in tumor progression, metastasis, resistance, and ultimately treatment failure, hypoxia is emerging as a significant, high-priority target for cancer therapy. As our prodrugs are designed to undergo selective activation under conditions of tumor hypoxia, we anticipate that they should have a favorable safety profile and produce less toxicity to normal tissues at the doses that are effective in treating tumors than is the case with traditional therapies.

We have generated clinical data with TH-302 alone and administered in combination with multiple anticancer drugs and in multiple cancer types. Drugs that we have tested or are currently evaluating in combination with TH-302 include chemotherapies (e.g., doxorubicin, gemcitabine, docetaxel, pemetrexed, bortezomib) and antiangiogenics (e.g., pazopanib, bevacizumab, sorafenib, and sunitinib). The current total market addressed by these drugs exceeds $10 billion. We have tested or are currently evaluating TH-302 in indications including soft tissue sarcoma, pancreatic cancer, head and neck cancer, lung cancer, melanoma, prostate cancer, glioblastoma, kidney cancer, liver cancer, gastrointestinal stromal tumors, multiple myeloma, and leukemia. In the U.S. alone, new cases of these cancers exceed 840,000 per annum.

The table below depicts the latest estimates from the American Cancer Society on expected 2013 incidence and deaths for cancers in the United States that we consider therapeutic areas of interest for TH-302.

Type of Cancer	New Cases	Deaths
Prostate cancer	238,590	29,720
Lung cancer	228,190	159,480
Melanoma	76,690	9,480
Kidney	65,150	13,680
Head and Neck	53,640	11,520
Leukemia (all)	48,610	23,720
Pancreatic cancer	45,220	38,460
Liver (& intrahepatic bile duct)	30,640	21,670
Brain (& other nervous system)	23,130	14,080
Multiple myeloma	22,350	10,710
Soft tissue sarcoma (including heart)	11,410	4,390

The market opportunity for our two most advanced clinical development programs with TH-302 in soft tissue sarcoma and pancreatic cancer are described below.

Soft Tissue Sarcoma

Sarcomas are a group of aggressive cancers originating in the supporting tissues of the body (e.g. muscle, fat, blood vessels or in any other tissue that surrounds and protects the organs of the body). There are currently limited treatment options for sarcomas. Soft tissue sarcomas are treated with surgery, chemotherapy and radiation. Usually a combination of these modalities offers the best chance to treat the disease successfully. Doxorubicin and ifosfamide are the most commonly used chemotherapeutic agents in patients with advanced soft

tissue sarcoma, but response rates are generally low and toxicity can be significant. Doxorubicin administered as monotherapy is associated with an overall survival rate of approximately 8 months to 12 months, and an overall response rate of approximately 15% to 25%, but is limited in use due to cumulative cardiotoxicity.

Pancreatic Cancer

It is estimated that approximately 45,000 cases of pancreatic cancer are diagnosed in the U.S. every year. Pancreatic cancer is the eleventh most common in the U.S. Almost 67% of cases are diagnosed in people aged 65 and over; it is uncommon in people under the age of 40. Pancreatic cancer has a low survival rate regardless of stage of disease, with almost 95% of patients dying from their disease within 5 years. It is estimated that there are around 38,000 deaths from pancreatic cancer in the U.S. alone each year.

Gemcitabine is the current standard of care for patients with pancreatic cancer and is associated with a median overall survival of approximately 6 months and an overall response rate of approximately 10%. Erlotinib, the only other therapeutic approved for the first line of treatment of patients with pancreatic cancer, was shown in its registrational Phase 3 study in combination with gemcitabine to convey a median overall survival of 6.24 months and overall response rate (complete plus partial response rate) of 8.6%.

Glufosfamide

From 2004 through 2009 we conducted clinical development of glufosfamide, a drug candidate that shares certain structural characteristics with glucose but acts instead as a chemotherapeutic agent when taken up by a cell. In October 2009, we entered into an exclusive license agreement with Eleison Pharmaceuticals, Inc. (“Eleison”). Pursuant to the agreement we granted Eleison exclusive worldwide rights to develop and commercialize glufosfamide for the treatment of cancer in humans and animals, and certain other uses. Under the agreement, Eleison is responsible for the development, manufacturing and marketing of glufosfamide. Eleison and Threshold will share equally in the profits of commercialization, if the further clinical development of glufosfamide leads to regulatory approval and marketing. Threshold has no further development plans for glufosfamide.

Discovery Research

We have research programs focused on better understanding the mechanism and maximizing the effectiveness of TH-302 in the treatment of cancer as well as identifying new therapeutic candidates that target the microenvironments of solid tumors and some hematological malignancies, particularly the severely hypoxic compartments. These extremely low oxygen conditions are not found in most normal tissues. The hypoxic zones of tumors are known to be resistant to standard chemotherapeutics and to radiation therapy. Hypoxia is also believed to contribute to more aggressive, invasive, and metastatic cancer phenotypes. Tumor hypoxia correlates with poor prognosis in cancer patients and is believed to represent a significant unmet medical need. The general nature of hypoxia in cancers offers the possibility for cancer therapeutics which are broadly useful in many indications with an associated large market opportunity. It is also now known that certain anticancer therapies (e.g. antiangiogenic agents) lead to an increase in tumor hypoxia and may support the combination of those therapies with hypoxia-targeted agents.

Our most advanced efforts targeting these regions are the design and development of novel hypoxia activated cytotoxic prodrug compounds. A prodrug is an inactive compound that is converted in the human body by enzymatic processes that result in the formation of an active drug. The prodrug concept is well established in chemotherapy and was initially only employed to modify the pharmacokinetic properties of compounds through non-specific activation processes. More recently the concept has been applied to the design of agents that are selectively activated in tumor tissues through specific activation processes.

Our prodrug candidates typically have two distinct parts, a toxic portion (the chemotherapeutic toxin) and an attached trigger molecule. To prevent general toxicity, the trigger molecule masks the toxin until the prodrug is

activated by the low oxygen concentration in the hypoxic zones of solid tumors and some hematological malignancies. Once activated, the toxin kills cells in its vicinity. We have designed prodrug candidates that are triggered only at the very low oxygen levels found in these hypoxic regions. Our experiments indicate that we can achieve a greater than 100-fold difference in cytotoxicity between cells in normal oxygen levels and hypoxic cells. Our lead investigational drug candidate, TH-302, was our first product candidate from this program. TH-302 is highly selective and produces a DNA cross-linking toxin upon activation. Hypoxia activated prodrugs of other toxin classes are being pursued. Lead compounds have demonstrated promising *in vitro* activity and additional characterization, evaluation and optimization of these compounds is currently underway.

Our expertise includes broad capabilities in chemical synthesis, biological assay development and*in vitro* and *in vivo* compound evaluation, formulation development, and pharmacology. Our medicinal chemistry expertise allows us to turn initially promising compounds generated by our chemists into drug candidates. We believe that our research focus combined with our integrated drug discovery platform provides us with the capacity to optimize our chances of successfully translating our laboratory observations with TH-302 to the clinic as well as to identify, discover and develop novel therapies for the treatment of cancer.

Manufacturing and Supply

The production of TH-302 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 ("API"), and final drug product of TH-302. Under our license and co-development agreement with Merck KGaA, we are dependent on Merck for clinical and commercial supply of TH-302, except for clinical trials for United States approval of TH-302 for soft tissue sarcoma and for any other clinical trials for which we are responsible. For these latter cases, we can obtain clinical supply directly from existing or new suppliers.

We are currently using contract manufacturers to manufacture TH-302 API and TH-302 drug product. We have plans to meet our clinical supply needs for 2013. We based our estimates for the amount of drug we will need on assumptions about trial enrollment and trial dose levels. If we are not successful in manufacturing sufficient quantities of TH-302 API and drug product or consume more drug product than anticipated because of a higher than expected trial utilization or have quality issues that limit the utilization of the drug product, we may experience a significant delay in our TH-302 clinical program.

Additional agreements for more supplies of each of our product candidates will be needed to complete clinical development and/or commercialize them. These products will need to satisfy all cGMP manufacturing requirements, including passing product specifications. Our inability to satisfy these requirements could delay our clinical programs.

During the years ended December 31, 2012, 2011 and 2010, we spent $18.8 million, $24.4 million and $18.9 million, respectively, on research and development, including product development, discovery research and contract manufacturing activities.

License and Development Agreements

Agreement with Merck KGaA

On February 3, 2012, we entered into a global license and co-development agreement with Merck KGaA, of Darmstadt, Germany, to co-develop and commercialize TH-302, our small molecule hypoxia-targeted drug. Under the terms of the agreement, Merck will receive co-development rights, exclusive global commercialization rights and will provide us an option to co-commercialize TH-302 in the United States. In exchange, we received an upfront payment of $25 million and received another $72.5 million in additional development milestones, including $42.5 million subsequent to December 31, 2012. We can earn additional potential milestone payments of $452.5 million, comprised of $112.5 million in regulatory and development milestones and $340 million in sales-based milestones.

In the United States, we will have primary responsibility for development of TH-302 in the soft tissue sarcoma indication. We and Merck KGaA will jointly develop TH-302 in all other cancer indications being pursued. Merck KGaA will pay 70% of worldwide development costs for TH-302. Subject to FDA approval in the United States, Merck KGaA will initially be responsible for commercialization of TH-302 while we will receive a tiered, double-digit royalty on sales. Under the royalty-bearing portion of the agreement, we retain the option to co-promote TH-302 in the United States. Additionally, we retain the option to co-commercialize TH-302 upon the achievement of certain sales or regulatory milestones, allowing us to participate in up to 50% of the profits in the United States depending on total sales. Outside of the United States, Merck KGaA will be solely responsible for the commercialization of TH-302 while we will receive a tiered, double-digit royalty on sales in these territories. The agreement became effective on March 12, 2012, upon termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. The agreement will continue on a country-by-country basis until the later of the last to expire patent covering TH-302 in such country or ten years following the commercial launch of a product containing TH-302 in such country, unless terminated earlier. Merck has the right to terminate the agreement after the achievement of certain milestones, and each party has the right to terminate the agreement following uncured material breach by the other party.

Agreement with Eleison Pharmaceuticals, Inc.

On October 14, 2009, we entered into an exclusive license agreement with Eleison Pharmaceuticals, Inc. ("Eleison"). Pursuant to the agreement we granted Eleison exclusive worldwide rights to develop and commercialize glufosfamide for the treatment of cancer in humans and animals, and certain other uses. Under the agreement, Eleison is responsible for the development, manufacturing and marketing of glufosfamide. Eleison and Threshold will share equally in the profits of commercialization, if the further clinical development of glufosfamide leads to regulatory approval and marketing.

Eleison will pay us 50% of its profits from commercialization on a quarterly basis, beginning on the date of first commercial sale, if any. Eleison has the right to sublicense some or all of its rights under the agreement, and will pay us 50% of amounts received under any sublicenses, including, without limitation, any royalty payments, license fee payments, milestone payments and payments for any equity or debt purchases by a sublicensee, within 30 days of the receipt of any such amounts or payments by Eleison. Eleison will bear all costs associated with development, commercialization and patent prosecution, and will control product development and commercialization. In addition, Eleison will be responsible for all royalty and milestone payments due under the Baxter license and MediBIC development agreement. The agreement contemplates that Eleison, to satisfy its diligence obligations, will raise sufficient funds to commence clinical development activities with glufosfamide. In 2011, we received a $0.1 million payment, which represents our 50% share of an upfront payment from a sublicense by Eleison.

In the event that Eleison fails to satisfy its diligence obligations, we may, at our option, terminate the agreement for material breach or convert the license granted under the agreement to a non-exclusive license.

The agreement will remain in effect as long as Eleison continues to sell glufosfamide anywhere in the world or receives payments under any sublicenses. Each party is entitled to terminate the agreement upon the other party's material breach after expiration of a 60-day cure period (30 days in the event of a payment breach). Each party is entitled to terminate the agreement immediately upon the bankruptcy or similar petition of the other party that is not discharged within 60 days, or the assignment for the benefit of creditors by, or the appointment of a receiver over the property of, the other party. In addition, Eleison may terminate the agreement for convenience at any time on 90 days written notice to us.

Following any termination by Eleison for convenience or by us for Eleison's material breach, all licensed rights will revert to us. Following any termination by Eleison for our material breach, all licensed rights will fully vest in Eleison, provided that Eleison will be required to pay us 50% of the profit sharing payments it otherwise would have been required to pay us under the agreement.

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, 2012, we owned or held exclusive license to various United States and foreign patents and patent applications and Patent Cooperation Treaty patent applications relating to our research and development programs.

Our TH-302 product candidate and its use in the treatment of cancer are claimed in U.S. and corresponding foreign patents and patent applications in major market countries and are owned by us. We are seeking or have already obtained compound *per se* patent protection for TH-302 as well as claims directed to its use, alone and in combination with other cancer drugs, in the treatment of cancer. We also own other U.S., Patent Cooperation Treaty, and foreign patent applications relating to the results of our research on hypoxia-activated prodrugs and their use as cancer drugs and related reagents and methods.

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 pending patent applications will result in the issuance of any patents. 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 and certain of our 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 pharmaceutical 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, if our product candidates are commercialized, then 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. 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.

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 TH-302 product candidate for targeting the tumor hypoxia may eventually compete with other companies who are developing or were developing drugs that target tumor hypoxia such as Proacta Incorporated. A number of biotechnology and pharmaceutical companies are marketing and/or developing cancer therapeutics competing in prostate, lung, pancreatic, melanoma and soft tissue sarcoma. Such companies include: AstraZeneca PLC, Genentech, Inc., Bristol-Myers Squibb Company, Eli Lilly and Company, GlaxoSmithKline plc, Bayer Pharmaceuticals, Hoffmann-LaRoche, Inc., Infinity Pharmaceuticals, Johnson & Johnson, Onyx Pharmaceuticals, Inc., Merck KGaA, Novartis AG, Pfizer, Inc., Amgen Inc., Clovis Oncology, ImClone Systems, Inc., Millennium Pharmaceuticals, Inc., OSI Pharmaceuticals, Inc., Telik, Inc., Sanofi-Aventis U.S., Sunesis Pharmaceuticals, Inc., Plexxikon Inc., Celgene Corporation, ARIAD Pharmaceuticals, Inc. and ZIOPHARM Oncology, Inc.

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 investigation new drug application or IND, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use;
- pre-approval inspection of manufacturing facilities and selected clinical investigators; and
- FDA approval of a new drug application or NDA, or of an 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, expose 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 be cleared 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 the hold is lifted and 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. Regulatory authorities may require additional data before allowing the clinical trials to commence or proceed from one Phase to another, and could demand that the trials 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 clinical trial.

Clinical Trials

Clinical trials for new drug candidates are typically conducted in three sequential phases that may overlap. Phase 1 trials involve the initial introduction of the drug candidate into humans and are conducted in volunteers or in patients with a specific disease depending on the intended use of the drug and its potential safety profile. The emphasis in Phase 1 is on testing for safety (adverse effects), dosage, tolerance, absorption, metabolism, distribution, excretion, and preliminary clinical pharmacology. Phase 2 clinical trials involve 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. When a compound shows evidence of effectiveness along with an acceptable safety profile in Phase 2 clinical trials the drug is moved to Phase 3 development. Phase 3 clinical trials are undertaken to more fully evaluate the safety and efficacy and to establish the overall risk/benefit profile of the drug. These Phase 3 clinical trials are the basis for determining if the drug should be registered. During all clinical trials, physicians monitor patients to determine effectiveness of the drug candidate and observe and report any adverse effects 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 or that the drug is not sufficiently efficacious to continue further studies.

The data from the clinical trials, together with preclinical data and other supporting information that establishes a drug candidate's safety profile and efficacy, are submitted to the FDA in the form of an 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 assessment is reviewed within 60 days following submission of the NDA. If deemed acceptable, the FDA will "file" the NDA, thereby initiating the review clock triggering substantive review of the application. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal substantive review goals of six months for priority NDAs (for drugs addressing serious or life threatening conditions for which there is an unmet medical need) and ten months for regular NDAs. The FDA, however, is not legally required to complete its review within these periods, and these performance goals may change over time. Following a complete assessment of the application the FDA will issue an "action letter" that can be an approval, a request for additional information needed to approve the drug or a rejection letter (no approval).The FDA's review of an NDA may involve review and recommendations by an independent FDA advisory committee. The FDA may deny approval of an 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 that 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 that 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 post approval studies may be made a condition to be satisfied after a drug receives approval especially in the case of an accelerated approval. The results of post approval 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. The product may be subject to withdrawal of the approval if effectiveness is not confirmed in the Phase 4 studies. 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 and is specifically included in drug labeling. While 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, manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. Failure to comply with FDA requirements can result in adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties.

Special Protocol Assessments

A clinical trial sponsor may submit a request for a special protocol assessment (SPA) from the FDA. Under the SPA procedure, a sponsor may seek the FDA's agreement on the design and size of a clinical trial intended to form the primary basis of an effectiveness claim. If the FDA agrees in writing, its agreement may not be changed after the trial begins, except in limited circumstances, such as when a substantial scientific issue essential to determining the safety and effectiveness of a product candidate is identified after a Phase 3 clinical trial is commenced and agreement is obtained with the FDA. If the outcome of the trial is successful, the sponsor will ordinarily be able to rely on it as the primary basis for approval with respect to effectiveness. The FDA, however, may make an approval decision based on a number of factors, including the degree of clinical benefit, and the FDA is not obligated to approve an NDA as a result of an SPA, even if the clinical outcome is positive.

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 an 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.

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 an NDA, plus the time between the submission date of an 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 an 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, an 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 trials 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 control data. The Hatch-Waxman Amendments also instituted a third type of drug application that requires the same information as an 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, 2012, we had 48 full-time employees, including 18 who hold Ph.D. and/or M.D. degrees. Thirty six 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 170 Harbor Way Suite 300 South San Francisco 94080. 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 Exchange Act. 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 http://www.sec.gov. The materials are also available at the SEC's Public Reference Room, located at 100 F Street, Washington, D.C. 20549. The public may obtain information through the public reference room by calling the SEC at 1-800-SEC-0330.

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

ITEM 1A. RISK FACTORS

Risks Related to Drug Discovery, Development and Commercialization

We are substantially dependent upon the success of TH-302.

We have focused our development activities on TH-302, and we do not presently have other compounds in clinical development. The failure of TH-302 to achieve successful clinical trial endpoints, delays in clinical or development of TH-302, unanticipated adverse side effects related to TH-302 or any other adverse developments or information related to TH-302 would significantly harm our business and the value of our common stock.

We are dependent upon our collaborative relationship with Merck KGaA to further develop, manufacture and commercializeTH-302.

Our success in developing, manufacturing and commercializing TH-302 will depend on our relationship with Merck KGaA. On February 3, 2012, we entered into a global license and co-development agreement with Merck KGaA to co-develop and commercialize TH-302. In the United States, we have primary responsibility for development of TH-302 in the soft tissue sarcoma indication. Threshold and Merck KGaA will jointly develop TH-302 in all other cancer indications being pursued, with Merck having primary responsibility. Threshold has rights to co-promote TH-302 in the United States, which it can exercise by giving notice during specified periods, and has the right to co-commercialize TH-302 if certain development or sales milestones are achieved.

We are subject to a number of risks associated with our dependence on our collaborative relationship with Merck, including:

- our ability, together with Merck, to achieve developmental and commercial milestones that will trigger payments to Threshold under the agreement;
- our ability to fund thirty percent (30%) of the global development expenses of TH-302;
- decisions by Merck regarding the amount and timing of resource expenditures for the development and commercialization of TH-302;
- possible disagreements with Merck as to development plans, clinical trials, regulatory marketing or sales;
- our need to develop a sales force to co-promote or co-commercialize TH-302 in the United States if we chose to do so, or our reliance on Merck to promote TH-302 in the United States;
- our inability to co-promote or co-commercialize TH-302 in any country outside the United States, which makes us solely dependent on Merck to promote and commercialize TH-302 in foreign countries;
- Merck's right to terminate the collaboration agreement on limited notice after the attainment of certain milestones or in certain circumstances involving our insolvency or material breach of the agreement;
- loss of significant rights if we fail to meet our obligations under the collaboration agreement;
- adverse regulatory or legal action against Merck resulting from failure to meet healthcare industry compliance requirements in the promotion and sale of TH-302, including federal and state reporting requirements;
- changes in key management personnel at Merck, including Merck's representatives on the joint steering committee or other committees that are administering the agreement; and
- possible disagreements with Merck regarding interpretation or enforcement of the agreement.

We have limited ability to direct Merck in its development of TH-302 and we may be unable to obtain any remedy against Merck if they fail to do so, or do so in a manner that we think is inadequate. Merck may not have sufficient expertise to develop, promote or obtain reimbursement for oncology products in the United States and

may fail to devote appropriate resources to this task. Merck's development plans may be slower than or different from our plans were, when we were developing TH-302 on our own, leading to changes and delays in development and in the achievement of milestones that would impact payments to us under our agreement with Merck. In addition, Merck may establish a sales and marketing infrastructure for TH-302 that is not appropriate for the sales opportunity or establish this infrastructure too early or late in view of the ultimate timing of potential regulatory approvals. We are at risk with respect to the success or failure of Merck's development and commercial decisions related to TH-302 as well as the extent to which Merck succeeds in the execution of its strategy. Merck's development of other products may affect its incentives to develop and commercialize TH-302 and cause it to take actions that may be different from those we would take.

Under the terms of the agreement, we and Merck must agree on the development plan for TH-302. If we and Merck cannot agree, clinical trial progress could be significantly delayed. Further, if we cease funding development of TH-302 under the collaboration agreement, then we will be entitled to receive a royalty, but will lose our right to co-commercialize TH-302 and share in profits.

Merck has the right to terminate the agreement after certain milestones have been met on ninety (90) days prior written notice, or following our uncured material breach. If Merck terminates the agreement, then we shall become responsible for the costs of development and commercialization of TH-302, and there can be no assurance we would be able to do so, or to find another collaborator for the continued development and commercialization of TH-302.

If we are unable to maintain our collaborative relationship with Merck, we may be unable to continue development, manufacturing and marketing activities at our own expense. If we were able to do so on our own, this would significantly increase our capital and infrastructure requirements, would necessarily impose delays on development programs, may limit the indications we are able to pursue and could prevent us from effectively developing and commercializing TH-302.

Disputes with Merck may delay or prevent us from further developing, manufacturing or commercializingTH-302, and could lead to litigation against Merck, which could be time consuming and expensive.

Delays in our clinical trials could result in us not achieving anticipated developmental milestones when expected, increased costs and delay our ability to obtain regulatory approval and commercialize our product candidates.

Delays the progression of our clinical trials could result in us not meeting previously announced clinical milestones and could materially impact our product development costs and milestone revenue and delay regulatory approval of our product candidates. We do not know whether planned clinical trials will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including:

- adverse safety events experienced during our clinical trials;
- a lower than expected frequency of clinical trial events;
- delays in obtaining clinical materials;
- slower than expected patient recruitment to participate in clinical trials;
- delays in reaching agreement on acceptable clinical trial agreement terms with prospective sites or obtaining institutional review board approval,
- delays in obtaining regulatory approval to commence new trials;
- changes to clinical trial protocols; and
- disagreements with Merck KGaA on development plans.

Delays in clinical trials can also result from difficulties in enrolling patients in our clinical trials, which could increase the costs or affect the timing or outcome of these clinical trials. This is particularly true with respect to diseases with relatively small patient populations. Timely completion of clinical trials depends, in addition to the factors outlined above, on our ability to enroll a sufficient number of patients, which itself is a function of many factors, including:

- the therapeutic endpoints chosen for evaluation;
- the eligibility criteria defined in the protocol;
- the perceived benefit of the investigational drug under study;
- the size of the patient population required for analysis of the clinical 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.

If we do not successfully complete our clinical trials on schedule, the price of our common stock may decline.

Although we obtained a special protocol assessment for TH-302 for soft tissue sarcoma, a special protocol assessment does not guarantee any particular outcome from regulatory review, including any regulatory approval.

We have obtained an agreement with the Food and Drug Administration, or FDA, following a special protocol assessment, or SPA, for the registration trial for TH-302 for the treatment of soft tissue sarcoma in the United States. The SPA process allows for FDA evaluation of a clinical trial protocol intended to form the primary basis of an efficacy claim in support of a new drug application, or NDA, and provides a product sponsor with an agreement confirming that the design and size of a trial will be appropriate to form the primary basis of an efficacy claim for an NDA if the trial is performed according to the SPA. Even if we believe that the data from a clinical trial are supportive, an SPA is not a guarantee of approval, and we cannot be certain that the design of, or data collected from, a trial will be adequate to demonstrate safety and efficacy, or otherwise be sufficient to support regulatory approval. There can be no assurance that the terms of an SPA will ultimately be binding on the FDA, and the FDA is not obligated to approve an NDA, if any, even if the clinical outcome is positive. The FDA retains significant latitude and discretion in interpreting the terms of an SPA and the data and results from a clinical trial, and can require trial design changes or additional studies if issues arise essential to determining safety or efficacy. Data may subsequently become available that causes the FDA to reconsider the previously agreed upon scope of review and the FDA may have subsequent safety or efficacy concerns that override an SPA, and we can give no assurance that as clinical trials proceed or as part of an NDA review process, if any, the FDA will determine that a previously approved SPA is still valid.

Additionally, an SPA may be changed only with written agreement of the FDA and sponsor, and any further changes we may propose to the protocol will remain subject to the FDA's approval. The FDA may not agree to any such amendment and, even if they agree, they may request other amendments to the trial design that could require additional cost and time, as well as increase the degree of difficulty in reaching clinical endpoints. As a result, even with an SPA, we cannot be certain that the trial results will be found to be adequate to support an efficacy claim and product approval.

Pre-clinical studies and Phase 1 or 2 clinical trials of TH-302 may not predict the results of subsequent human clinical trials.

Pre-clinical studies, including studies of our product candidates in animal models of disease, may not accurately predict the result of human clinical trials of those product candidates. In particular, promising animal studies suggesting the efficacy of TH-302 for the treatment of different types of cancer may not accurately predict the ability of TH-302 to treat cancer effectively in humans. TH-302 may be found not to be efficacious in treating cancer, alone or in combination with other agents, when studied in human clinical trials. In addition, we will not be able to commercialize our drug candidates 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 early clinical trials, including Phase 2 trials, does not ensure that later clinical trials will be successful. Our initial results from clinical trials of TH-302 in Phase 1 and Phase 2 clinical trials also may not be confirmed by later analysis or subsequent larger clinical trials. In particular, positive results for progression-free survival in the Phase 2b trial of TH-302 in pancreatic cancer may not predict the results of overall survival for patients in the same study or subsequent studies. A number of companies in the pharmaceutical industry, including us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

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

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

We cannot be certain 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 clinical testing may not be indicative of results in future clinical trials;
- clinical 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 and additional expense;
- 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.

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 certain 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.

Our product candidates are based on targeting the microenvironment of solid tumors and some hematological malignancies, which currently is an unproven approach to therapeutic intervention.

Our product candidates are designed to target the microenvironment of solid tumors and some hematological malignancies by, in the case of TH-302, harnessing hypoxia for selective toxin activation. We have not, nor to our knowledge has any other company, received regulatory approval for a drug based on this approach. We cannot be certain 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 these targeting approaches, 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.

Anti-tumor drugs being developed by us, including TH-302, are expected to have undesirable side effects. For example, in clinical trials of TH-302, some patients have exhibited skin and/or mucosal toxicities that have in some cases caused patients to stop or delay therapy. The extent, severity and clinical significance of these or other undesirable side effects may not be apparent initially and may be discovered or become more significant during drug development or even post-approval. These expected side effects or other side effects 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.

We have not yet gained sufficient experience with a commercial formulation of TH-302.

The formulation of TH-302 that we are using in our clinical trials was recently changed to address issues with a prior formulation that was subject to storage and handling requirements that were not be suitable for commercial product. The new formulation of TH-302 may be suitable for commercial product, but additional data will be required to verify this. There can be no assurance that it will be. If we are not able to develop a commercial formulation, we may delay registration of TH-302.

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.

For those drugs that meet the eligible requirements, we intend to seek orphan drug designation for the cancer indications that our drug 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.

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 were to be approved and receive orphan drug status, the FDA could 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 TH-302 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 or Merck KGaA fail to comply with continuing United States and foreign regulations, we or they 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 and Merck KGaA 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 used 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. Manufacturers of our products, if approved, will be subject to ongoing FDA requirements for submission of safety and other post-market information. If such 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;
- seize or detain products or require a product recall, or
- revise or restrict labeling and promotion.

The FDA and foreign regulatory authorities may 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 United States 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 clinical trial sponsors are required to post the general purpose of these clinical trials, as well as the eligibility criteria, location and contact information of the clinical trials. Since the establishment of this registry, there has been significant public debate focused on broadening the types of clinical 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 clinical trials that have been registered with a no-cost, publicly accessible database, such as http://www.clinicaltrials.gov. The Pharmaceuticals and Research Manufacturers of America has also issued voluntary principles for its members to make results from certain clinical trials 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 http://www.clinicaltrials.gov and to require the inclusion of clinical trial 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.

We do not have a sales force and may not develop an effective one.

Our license and co-development agreement with Merck KGaA gives us the right, under certain circumstances, to co-promote or co-commercialize TH-302. We have no sales experience, and developing a sales force will require substantial expenditures. We may not be able to effectively recruit, train or retain sales personnel. We may not be able to effectively sell TH-302, if approved, and if we exercise our rights to do so, 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 continue to incur significant losses for the foreseeable future, and our future profitability is uncertain.

We have incurred losses in each year since our inception in 2001, and we expect to incur losses for the foreseeable future. We have devoted, and will continue to devote for the foreseeable future, substantially all of our resources to research and development of our product candidates. For the year ended December 31, 2012, we had an operating loss of $20.0 million and a net loss of $71.1 million, including $51.2 million in non-cash expense related to the change in the fair value of outstanding warrants. Our cumulative net loss since our inception through December 31, 2012 was $323.3 million. Clinical trials and activities associated with discovery research are costly. We do not expect to generate any revenue from the commercial sales of our product candidates in the near term, and we expect to continue to have significant losses for the foreseeable future.

To attain ongoing profitability, we will need to develop products successfully and market and sell them effectively, or rely on other parties, such as Merck KGaA, to do so. We cannot predict when we will achieve ongoing profitability, if at all. We have never generated revenue from the commercial sales of our product candidates, and there is no guarantee that we will be able to do so in the future. If we fail to become profitable, or if we are unable to fund our continuing losses, we would be unable to continue our research and development programs.

Our financial results are likely to fluctuate from period to period, making it difficult to evaluate our stock based on financial performance.

Our quarterly and annual results of operations are likely to fluctuate based on the timing of milestones and payments under our license and development agreement with Merck KGaA. We believe that period-to-period comparisons of our operating results should not be relied upon as predictive of future performance. Our prospects must be considered in light of the risks, expenses and difficulties encountered by companies with no approved pharmaceutical products, and with products that are undergoing clinical development.

We are likely to require 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 lawsuits involving us or our product candidates.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund the Company's projected operating requirements for at least the next twelve months based upon current operating plans, milestone payment forecasts and spending assumptions. We expect that we will need to raise additional capital to support new in-house development programs or to in-license or otherwise acquire and develop additional products or programs. We intend to seek funds through additional arrangements with collaborators or others that may require us to relinquish rights to the products candidates that we might otherwise seek to develop or commercialize independently. We cannot be certain that we will be able to enter into any such arrangements on reasonable terms, if at all.

We may seek to raise capital through a variety of sources, including:

- the public equity market;
- private equity financing;
- collaborative arrangements;
- licensing arrangements; and/or
- public or private debt.

Our ability to raise additional funds will depend, in part on the outcome of our clinical trials and other clinical and regulatory events, as well as factors related to financial, economic, and market conditions, collaboration or license agreement with others and factors related to financial, economic and market conditions, many of which are beyond our control. We cannot be certain that sufficient funds will be available to us when required or on satisfactory terms, if at all. If adequate funds are not available, we may be required to significantly reduce or refocus our operations or to obtain funds through additional arrangements that may require us to relinquish rights to certain of our products, technologies or potential markets, any of which could delay or require that we curtail or eliminate some or all of our development programs or otherwise have a material adverse effect on our business, financial condition and results of operations. In addition, we may have to delay, reduce the scope of or eliminate some of our research and development, which could delay the time to market for any of our product candidates, if adequate funds are not available.

If we are unable to secure additional financing on a timely basis or on terms favorable to us, we may be required to cease or reduce certain research and development projects, to sell some or all of our technology or assets or to merge all or a portion of our business with another entity. Insufficient funds may require us to delay, scale back, or eliminate some or all of our activities, and if we are unable to obtain additional funding, there is uncertainty regarding our continued existence.

Our success depends in part on retaining and motivating key personnel and, if we fail to do so, it may be more difficult for us to execute our business strategy. As a small organization we are dependent on key employees and may 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 Senior Vice President of Discovery Research, Dr. Mark G. Matteucci. We do not have an employment agreement with Drs. Selick or Matteucci. The loss of the services of Drs. Selick or Matteucci 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 development of additional product candidates.

As of December 31, 2012, we had 48 employees. Our success will depend on our ability to retain and motivate remaining personnel and hire additional qualified personnel when required. 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 retention, motivation and recruitment efforts, we may be unable to execute our business strategy.

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 South San Francisco, 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-302. If these parties do not manufacture the active pharmaceutical ingredients or finished drug 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.

Under our license and co-development agreement with Merck KGaA, we are dependent on Merck for clinical and commercial supply of TH-302, except for clinical trials for United States approval of TH-302 for soft tissue sarcoma and for any other clinical trials for which we are responsible. In the latter case, we can obtain clinical supply directly from existing or new suppliers. Neither we nor Merck KGaA, have entered into any long term manufacturing or supply agreement for TH-302 or for any of our other 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 need to have sufficient TH-302 API and drug product to meet the clinical supply demands of our clinical trials. Additional clinical trial material continues to be manufactured as required. We have ordered additional API and drug product; however, we have experienced delays in the receipt of satisfactory drug product, and any additional delays we may experience in the receipt of satisfactory API or drug product could cause delays in our clinical trials, which would harm our business. In addition, we will need to obtain additional supplies of TH-302 API and drug product to complete our ongoing studies and any other additional trials. The need for additional supplies and preparation for registration may require scaling up and manufacturing process improvements in TH-302 API and drug product. The scaling up of the manufacturing processes for the TH-302 API may require facilities upgrades at our suppliers, which may lead to delays or disruption in supply, or delays in regulatory approval of TH-302. Changes to the formulation of TH-302 for our clinical trials may also require bridging studies to demonstrate the comparability of the new formulation with the old. These studies may delay our clinical trials and may not be successful. If we are not successful in procuring sufficient TH-302 clinical trial material, we may experience a significant delay in our TH-302 clinical program.

Merck will need to enter into additional agreements for additional supplies of TH-302 to complete clinical development and/or commercialize it or develop such capability itself. We cannot be certain that Merck can do so on favorable terms, if at all. The products will need to satisfy all current good manufacturing practice, or cGMP, regulations, including passing specifications. Merck’s inability to satisfy these requirements could delay our clinical programs.

If TH-302 or any of our other product candidates is approved by the FDA or other regulatory agencies for commercial sale, we or Merck as applicable, will need to have it manufactured in commercial quantities. It may

not be possible to increase the manufacturing capacity for TH-302 or any of our other 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 Merck with respect to TH-302, or we with respect to our other product candidates, are unable to successfully increase the manufacturing capacity for such 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 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 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 some of 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 may use clinical research organizations to assist in conduct of our 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 clinical trials conducted outside of the United States, where it may be more difficult to ensure that clinical trials are conducted in compliance with FDA requirements. 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 are dependent on Eleison to develop and commercialize glufosfamide

We are dependent upon Eleison Pharmaceuticals, Inc., to whom we exclusively licensed glufosfamide in October 2009, to develop and commercialize glufosfamide. Any profit sharing or other payments to us under the Eleison license depend almost entirely upon the efforts of Eleison, which may not be able to raise sufficient funds to commence clinical development activities with glufosfamide. Even if Eleison is successful at raising initial funding, it may not be successful in developing and commercializing glufosfamide or raising sufficient

funds for development and commercialization. We may also be asked to provide technical assistance related to the development of glufosfamide, which may divert our resources from other activities. If the Eleison license terminates in such a way that glufosfamide reverts to us and we seek alternative arrangements with one or more other parties to develop and commercialize glufosfamide, we may not be able to enter into such an agreement with another suitable third party or third parties on acceptable terms or at all.

Risks Related to Our Intellectual Property

Hypoxia activated prodrug technology is not a platform technology broadly protected by patents, and others may be able to develop competitive drugs using this approach.

Although we have US and foreign issued patents that cover certain hypoxia-targeted prodrugs, including TH-302, we have no issued patents or pending patent applications that would prevent others from taking advantage of hypoxia activated prodrug technology generally to discover and develop new therapies for cancer 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 hypoxia activated prodrug product candidates.

We are dependent on patents and proprietary technology. If we 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 to obtain and maintain patent protection sufficient to prevent others from marketing our product candidates, as well as to 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 their manufacture or use or if they are effectively protected by trade secrets. If our patent applications do not result in issued patents, or if our patents 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 may 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 might not have been the first to make the inventions covered by each of our pending patent applications and issued patents, and we may have to participate in expensive and protracted interference proceedings to determine priority of invention;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop identical, similar or alternative product candidates to any of our product candidates;
- our pending patent applications may not result in issued patents;

- our 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 patent claims to produce competitive products that fall outside the scope of our patents;
- we may not develop 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 the same or 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. Patent term extensions 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 certain aspects of 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 secret information 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 patents and patent applications, which are owned by third parties, exist in the general field of cancer therapies or in fields that otherwise may relate to our product candidates. 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 patent applications, unknown to us, which may later result in issued patents that our product candidates 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 pharmaceutical 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 drug product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. While we attempt to ensure that our active clinical investigational drugs and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties' patents and other proprietary rights, we cannot be certain 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, or the uses for which we intend to promote 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, AstraZeneca PLC, Genentech (a member of the Roche Group), Bayer Corporation, Celgene Corporation, Eli Lilly and Company and Pfizer, Inc. and from generic pharmaceutical manufacturers. In particular, our drug candidate for pancreatic cancer will compete with Gemzar®, marketed by Eli Lilly and Company, Tarceva®, cisplatin, paclitaxel, ifosfamide, and 5-flurouracil, or 5-FU, a generic product which is sold by many manufacturers. Several drugs marketed for different indications, such as Camptosar ®, marketed by Pfizer, Inc., Taxotere ®, marketed by Sanofi, DTIC-Dome®, marketed by Bayer Pharmaceuticals Corporation, Xeloda®, marketed by Hoffmann-LaRoche, Inc., Avastin ®, marketed by Genentech (a member of the Roche Group), Nexavar®, marketed by Onyx Pharmaceuticals, Inc. and Bayer AG, and Alimta®, marketed by Eli Lilly and Company, are under investigation or have completed investigation as combination therapies or monotherapy for pancreatic, prostate, ovarian, non-small cell lung and small cell lung cancers, melanoma and soft tissue sarcoma. In addition, Proacta Inc. has a compound under clinical investigation that targets the hypoxic zones of tumors, as our TH-302 clinical product candidate is intended to do. Celgene Corporation has completed its clinical trial and is seeking approval for Abraxene ® as a combination therapy for first-line treatment of pancreatic cancer. ZIOPHARM Oncology Inc. is conducting clinical trials of a compound as a combination therapy for first-line treatment of advanced soft tissue sarcoma.

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 expensive and 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 & 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.

Risks Related To Our Common Stock

A significant number of shares of our common stock are subject to issuance upon exercise of outstanding warrants, which upon such exercise would result in dilution to our security holders.

On March 16, 2011, we issued warrants to purchase an aggregate of 5,725,227 shares of our common stock, at an exercise price of $2.46 per share. On October 5, 2009, we issued warrants to purchase an aggregate of 7,329,819 shares of our common stock, at an exercise price of $2.23 per share, which exercise price was subsequently reduced to $2.05 per share on March 16, 2011 under the anti-dilution provisions of the warrants as a result of our March 2011 registered offering of common stock and warrants. In addition, on August 29, 2008, we issued warrants to purchase an aggregate of 3,588,221 shares of our common stock, at an exercise price of $2.34 per share, which exercise price was subsequently reduced to $1.86 per share on October 5, 2009 under the anti-dilution provisions of the warrants as a result of our October 2009 private placement. As of December 31, 2012, warrants to purchase 1,489,144 shares of common stock issued in March 2011, warrants to purchase 3,041,879 shares of common stock issued in October 2009 and warrants to purchase 529,410 shares of common stock issued in August 2008 had been exercised. The exercise price and/or the number of shares of common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including certain issuances of securities at a price equal to less than the then current exercise price (which could result from, for example, sales under our at market issuance sales agreement dated October 29, 2010 as amended), subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable. Although we cannot determine at this time which of these warrants will ultimately be exercised, it is reasonable to assume that such warrants will be exercised only if the exercise price is below the

market price of our common stock. To the extent the warrants are exercised, additional shares of our common stock will be issued that will be eligible for resale in the public market, which will result in dilution to our security holders. The issuance of additional securities could also have an adverse effect on the market price of our common stock.

The price of our common stock has been and may continue to be volatile.

The stock markets in general, the markets for biotechnology stocks and, in particular, the stock price of our common stock, have experienced extreme 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;
- announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;
- our or Merck's failure to meet milestones that would have given rise to payments under our agreement with Merck;
- announcements by Merck related to the development of TH-302 or announcements related to our agreement with Merck;
- 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; 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. Any such lawsuit could consume resources and management time and attention, which could adversely affect our business.

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 December 31, 2012, our officers, directors and other affiliates beneficially owned approximately 18.8% of our outstanding 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.

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 our board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

In addition, in August 2006, our board of directors adopted a preferred shares rights agreement, the provisions of which could make it more difficult for a potential acquirer to consummate a transaction without the approval of our board of directors.

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

We have never declared or paid cash dividends on our common stock. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

We may not maintain the listing of our common stock on the NASDAQ Capital Market.

Our ability to raise additional capital may be dependent upon our stock being quoted on the NASDAQ Capital Market. Previously, we had fallen out of compliance with continued listing requirements because our common stock did not comply with the $1.00 minimum bid price requirement for continued listing set forth in NASDAQ Marketplace Rule 5450(a)(1) (formerly Rule 4450(a)(5)). To regain compliance, effective August 20, 2008, we implemented a 1-for-6 reverse stock split of our common stock. After that date, our common stock traded above the minimum $1.00 bid price for at least ten consecutive business days and on September 5, 2008, the NASDAQ Stock Market notified us that we had regained compliance with the minimum bid price requirements. Even though we regained compliance with the minimum bid price, we cannot assure that we will be able to maintain compliance with the minimum bid price requirement or other listing requirements in the future, and our failure to do so could result in the delisting of our shares from the NASDAQ Capital Market.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

In July 2011, we entered into a noncancelable facility sublease agreement for 28,180 square feet of laboratory space and office space located in South San Francisco, California, which serves as our corporate headquarters. The lease began on October 1, 2011 and will expire on April 30, 2017. We had previously subleased approximately 67,905 square feet of laboratory and office space in Redwood City, California under an agreement that terminated in September 2011. We had previously leased an additional 6,489 square feet of laboratory space in Redwood City, California that terminated in August 2012. We believe our facilities are suitable and adequate for our current needs and that adequate facilities will be available to support our needs following termination of our existing leases.

ITEM 3. LEGAL PROCEEDINGS

None

ITEM 4. MINE AND SAFETY DISCLOSURES

Not applicable

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 Capital Market under the symbol "THLD" since August 20, 2008 and the NASDAQ Global Market from February 4, 2005 to August 19, 2008. 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 Capital Market and the NASDAQ Global Market for the periods indicated below, respectively. These prices do not include retail markups, markdowns or commissions.

	High	Low
Year Ended December 31, 2012:		
First Quarter	$9.07	$1.26
Second Quarter	$8.75	$5.88
Third Quarter	$9.28	$5.87
Fourth Quarter	$7.10	$3.95
Year Ended December 31, 2011:		
First Quarter	$3.34	$1.32
Second Quarter	$2.21	$1.40
Third Quarter	$2.22	$1.20
Fourth Quarter	$1.81	$1.18

We estimate that there were approximately 89 holders of record of our common stock as of February 28, 2013.

Dividends

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

Recent Sales of Unregistered Securities

None.

Use of Proceeds From Sale of Registered Securities

None

Equity Compensation Plans

The following table provides certain information with respect to all of our equity compensation plans in effect as of December 31, 2012:

	Number of securities to be issued upon exercise of outstanding options	Weighted-average exercise price of outstanding options	Number of securities remaining available for future issuance under equity compensation plans (1)(2)
Equity compensation plans approved by stockholders	5,098,972	$ 3.18	801,552
Equity compensation plans not approved by stockholders	—	—	—
Total	5,098,972	$ 3.18	801,552

(1) Includes 303,141 shares of common stock issuable under our 2004 Employee Stock Purchase Plan.

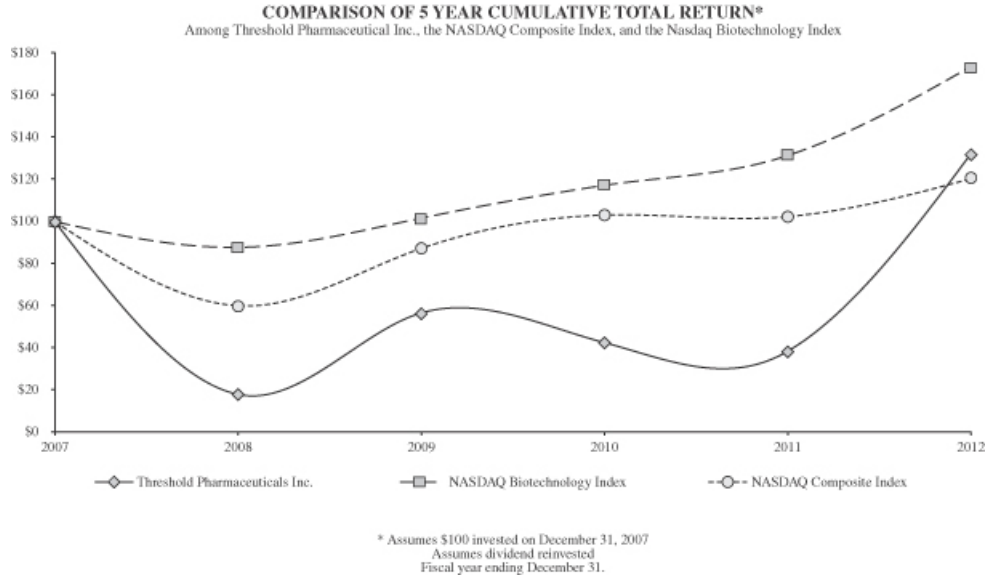
(2) On January 1, 2011, and annually thereafter, the authorized shares for the 2004 Equity Incentive Plan is automatically increased by a number of shares equal to the lesser of:

- 5% of the number of our shares issued and outstanding prior to the preceding December 31;
- 1,250,000 shares; or
- an amount determined by our board of directors.

Stock Performance Graph

The following graph shows the total stockholder return of an investment of $100 in cash on December 31, 2007 for (i) Threshold Pharmaceuticals, Inc. common stock; (ii) the NASDAQ Composite Index; and (iii) the NASDAQ Biotechnology Index through December 31, 2012. Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends; however no dividends have been declared on our common stock to date. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

This section is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



ITEM 6. SELECTED FINANCIAL DATA

The following tables reflect selected consolidated summary financial data for each of the last five fiscal years and are derived from our audited financial statements. This data should be read in conjunction with Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and Part II, Item 8, "Financial Statements and Supplementary Data", appearing elsewhere in this Annual Report on Form 10-K. In August 2008, our Board of Directors approved a 1-for-6 reverse split of its common stock, effective August 20, 2008. Accordingly, all references to common shares of stock and net loss per common share have been retroactively adjusted to reflect the reverse split.

	Years Ended December 31,				
	2012	2011	2010	2009	2008
	(In thousands, except per share data)				
Revenue	$ 5,867	$ 62	$ —	$ —	$ 1,440
Operating expenses:					
Research and development (1)	18,786	24,388	18,937	15,844	13,440
General and administrative (1)	7,080	5,710	4,971	5,480	6,734
Total operating expenses	25,866	30,098	23,908	21,324	20,174
Loss from operations	(19,999)	(30,036)	(23,908)	(21,324)	(18,734)
Interest income (expense), net	80	25	60	(13)	442
Other income (expense), net	(51,216)	4,358	5,166	(2,311)	—
Net loss	$(71,135)	$(25,653)	$(18,682)	$(23,648)	$(18,292)
Net loss per common share:					
Basic and diluted	$ (1.31)	$ (0.56)	$ (0.56)	$ (1.21)	$ (1.97)
Weighted average number of shares used in net loss per common share calculations:					
Basic and diluted	54,219	45, 900	33,654	19,594	9,275
(1) Includes employee and non-employee non-cash stock-based compensation of:					
Research and development	$ 1,521	$ 471	$ 381	$ 1,003	$ 1,504
General and administrative	$ 1,489	$ 568	$ 422	$ 1,208	$ 1,748

	As of December 31,				
	2012	2011	2010	2009	2008
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 70,848	$20,290	$14,699	$37,315	$22,337
Working capital	70,198	11,953	12,129	34,783	20,292
Total assets	89,521	22,436	16,204	48,685	24,531
Total liabilities	103,374	17,953	11,261	26,028	3,117
Total stockholders' equity (deficit)	(13,853)	4,483	4,943	22,657	21,414

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 using our expertise in the tumor microenvironment to discover and develop therapeutic agents that selectively target tumor cells for the treatment of patients living with cancer. Our lead investigational small molecule, TH-302, is being evaluated in two pivotal Phase 3 clinical trials and multiple earlier-stage clinical trials. We have a global license and co-development agreement for TH-302 with Merck KGaA, with an option to co-commercialize in the United States. TH-302 was discovered by our scientists based on our hypoxia-activated prodrug ("HAP") technology. Hypoxia, or abnormally low oxygen concentration, is a common feature of the tumor microenvironment in most solid tumors and in the bone marrow of patients with some hematological malignancies (also known as blood cancers, for example, leukemias and multiple myeloma). Tumor hypoxia is associated with the development of resistance to traditional anticancer treatments, including chemotherapy and radiotherapy, enhanced metastatic potential, and ultimately treatment failure. Normal healthy tissues, in contrast, are well oxygenated and typically are not hypoxic. As a prodrug, TH-302 is designed to remain essentially inactive in normal tissues, but to activate under conditions of tumor hypoxia. Upon activation, TH-302 releases bromo isophosphoramide mustard (Br-IPM), a potent cytotoxin that kills cells by causing DNA to crosslink. We believe that by virtue of targeting tumor hypoxia, TH-302 has broad clinical applicability across many types of solid tumors and some hematological malignancies. To explore this broad therapeutic potential of TH-302, we are conducting multiple clinical trials to evaluate its safety and efficacy as monotherapy and in combination with currently marketed anticancer drugs, including traditional chemotherapeutic agents and antiangiogenic agents.

TH-302 is currently in Phase 1, Phase 2 and Phase 3 clinical trials. The development plan for TH-302 is designed to investigate the efficacy and safety across a broad range of solid tumors and hematologic malignancies. We reported updated top-line results from the initial Phase 1 monotherapy trial of TH-302 (401 trial) including indication specific data in patients with metastatic melanoma and small-cell lung cancer (SCLC). We have also reported results from each of four Phase 1/2 combination therapy investigations of a chemotherapy agent plus TH-302 in solid tumors involving combining TH-302 with doxorubicin, gemcitabine, docetaxel and pemetrexed. We have also reported results from our clinical study of TH-302 in patients with advanced leukemias (407 trial) and initiated a clinical study of TH-302 in patients with multiple myeloma (408 trial). In addition, investigations have been initiated to explore the combination of TH-302 with antiangiogenic therapies including a Phase 1/2 dose escalation clinical trial of TH-302 in combination with sunitinib (Sutent ®) in patients with advanced renal cell carcinoma or gastrointestinal stromal tumors (410 trial) and physician initiated clinical trial of TH-302 administered either in combination with bevacizumab (Avastin ®) in patients with recurrent high grade astrocytoma including glioblastoma or in combination with pazopanib (Votrient ®) in patients with solid tumors. In September 2012, European Society for Medical Oncology (ESMO) 2012 Congress in Vienna, Austria we announced preliminary data from the physician initiated clinical trial of TH-302 in combination with bevacizumab in patients with recurrent glioblastoma.

In February of 2012 we reported top-line results from the randomized and controlled Phase 2 trial of TH-302 plus gemcitabine in patients with pancreatic cancer (404 trial). The median progression-free survival progression free survival was 5.6 months for patients treated with gemcitabine in combination with TH-302 at 240 mg/m2 and 340 mg/m2 compared to 3.6 months for patients treated with gemcitabine alone. The progression free survival hazard ratio comparing the TH-302 combination to gemcitabine alone was 0.61 (95% confidence

interval: 0.43—0.87) which was highly statistically significant (p = 0.005) and represented a 63% improvement in progression free survival. The response rate in the combination arms was 22% compared to 12% in the gemcitabine alone group. Results also demonstrated greater efficacy in the higher TH-302 dose group compared to the lower dose group. The combination had a safety profile that was consistent with our prior study of this combination regimen. As in that study, skin and mucosal toxicities related to TH-302 were dose dependent but not dose limiting. In April 2012, we provided detailed results from our 404 trial at the American Association of Cancer Research (AACR) annual meeting including results for each of the 240 mg/m2 and 340 mg/m2 TH-302 combination arms. The median progression free survival was 6.0 months in the 340 mg/m2 group. The response rate was 27% in the 340 mg/m2 group. A similar dose dependency was reported in serum CA19-9 levels. There was greater drug exposure in the combination groups with a median of 4 cycles received with gemcitabine alone compared with 5 cycles in the 240 mg/m2 group and 6 cycles in the 340 mg/m2 group. The combination safety profile was consistent with the prior study of this combination regimen. As in that study, skin and mucosal toxicities were less than what had been seen at the single-agent maximum tolerated dose of TH-302, which was previously established at 575 mg/m2. The incidence of Grade 3/4 thrombocytopenia and Grade 3/4 neutropenia was significantly higher in the combination arms and highest in the 340 mg/m2 group. Discontinuations for adverse events were lowest however in the 340 mg/m2 group. In September 2012, at ESMO 2012 Congress, updated results were presented confirming a significant improvement (p=0.008) in progression free survival. The updated progression free survival hazard ratio comparing the TH-302 combinations to gemcitabine alone was 0.64 (95% confidence interval: 0.45—0.89). This was associated with a 2.4-month increase in median progression free survival for patients receiving TH-302 340 mg/m^2. New findings from the Phase 2b trial were presented including an analysis of overall survival, which was a secondary endpoint of the study. This analysis indicated that patients treated with gemcitabine alone had a median overall survival of 6.9 months compared with 9.2 months for patients treated with 340 mg/m2 TH-302 plus gemcitabine (HR: 0.955, 95% CI: 0.67-1.37, p=0.800) and 8.7 months for patients treated with 240 mg/m2 TH-302 plus gemcitabine (HR: 0.960, 95% CI: 0.67-1.38, p=0.827). While not statistically significant, the improvement in median overall survival is consistent with the improvement in median progression free survival reported previously. The trial was not designed to detect a statistically significant improvement in overall survival and included a cross-over component. Patients receiving gemcitabine alone who crossed over to receive gemcitabine plus TH-302 upon disease progression contributed to an increase in survival of the control arm. TH-302 continued to demonstrate a safety profile consistent with what had been previously reported at AACR. The most common adverse events were fatigue, nausea, constipation and peripheral edema, and were similar across groups. Skin and mucosal toxicities and myelosuppression were the most common adverse events related to TH-302, were mostly Grade 1 and 2, and did not result in increases in treatment discontinuation. Adverse events leading to discontinuation of study treatment as well as serious adverse events were balanced across all treatment arms. Grade 3/4/5 adverse events were generally below 10%. In December 2012, Merck KGaA opened MAESTRO a global Phase 3 trial of TH-302 plus gemcitabine in patients with pancreatic cancer. MAESTRO stands for TH-302 in the treatment of MetastAtic or unrESectable pancreaTic adenocaRcinOma.

In 2011, we presented updated top-line results from our Phase 1/2 combination therapy in patients with soft tissue sarcoma treated with doxorubicin plus TH-302 at the maximum tolerated dose of 300 mg/m 2 (403 trial). We also provided additional data from the maintenance component as well as an update on the overall efficacy of the Phase 2 component of the 403 trial at the 17th CTOS Annual Meeting in November 2012. In February 2011, we reached agreement with the FDA on the design and planned analysis of a pivotal Phase 3 trial in patients with soft tissue sarcoma (406 trial). As part of the Special Protocol Assessment (SPA) submission, the FDA agreed that the design and planned analysis of the proposed Phase 3 trial adequately addresses the objectives necessary to support a regulatory submission. We initiated the pivotal Phase 3 trial in September of 2011 and currently expect to complete enrollment around the end of 2013.

We are working to broaden the applicability of TH-302 to other cancers and in combination with other approved anti-cancer drugs as well as to discover additional hypoxia activated prodrugs that will selectively target cancer cells.

We were 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 commercial sales of our product candidates, and prior to our entering into a collaboration agreement with Merck KGaA in February 2012, we have funded our operations through the private public placement and public offerings of our equity securities. On February 3, 2012, we entered into an agreement with Merck KGaA, which to date has provided for $97.5 million in upfront and milestone payments, including $42.5 million received subsequent to December 31, 2012. We expect to receive additional $12.5 million in potential milestone payments in 2013. During the year ended December 31, 2012, we sold 2,022,144 shares of common stock under our at market issuance sales facility for net proceeds of $12.3 million, and we received approximately $8.8 million from the exercise of warrants to purchase common stock. As of December 31, 2012 we had cash, cash equivalents and marketable securities of $70.8 million. For the year ended December 31, 2012, we had an operating loss of $20.0 million and a net loss of $71.1 million, including $51.2 million in non-cash expense related to the change in the fair value of outstanding warrants. Our cumulative net loss since our inception through December 31, 2012 was $323.3 million.

We expect to continue to devote substantial resources to research and development in future periods as we complete our current clinical trials, start additional clinical trials and continue our discovery efforts. Research and development expenses net of reimbursements of Merck's 70% share of total TH-302 development expenses, are expected to increase in 2013 compared to 2012 due to the continued execution of existing clinical trials and beginning of new clinical trials. We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our projected operating requirements for at least the next twelve months based upon current operating plans, milestone payment forecasts and spending assumptions. We expect that we will need to raise additional capital to support new in-house development programs or to in-license or otherwise acquire and develop additional products or programs. We intend to seek funds through additional 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. Research and development expenses may fluctuate significantly from period to period as a result of the progress and results of our clinical trials.

Revenue

We have not generated any revenue from the commercial sales of our product candidates since our inception and do not expect to generate any revenue from the commercial sales of our product candidates in the near term. We recognized revenue of $5.9 million during the year ended December 31, 2012, from the amortization of the $67.5 million in upfront and milestone payments earned in 2012 from our collaboration with Merck KGaA. We are amortizing the upfront and milestone payments over the period of performance (product development period). We will periodically review and, if necessary, revise the estimated periods of performance of our collaboration. In 2011, we recognized $0.1 million in revenue in connection with our 2009 agreement with Eleison Pharmaceuticals ("Eleison") for the development of glufosfamide, which represents our 50% share of an upfront payment from a sublicense by Eleison.

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.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for our personnel in the executive, public relations, finance, patent, corporate development 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 market research and recruiting. Other costs include professional fees for legal and accounting services, insurance and facility costs.

Stock-Based Compensation

We recognize stock-based compensation in accordance with the fair value provisions of Accounting Standard Codification ("ASC") 718,*"Compensation—Stock Compensation."* Refer to the discussion of accounting treatment of stock based compensation below under***Critical Accounting Policies***.

Results of Operations for the Years Ended December 31, 2012 and 2011

Revenue

For the year ended December 31, 2012, we recognized $5.9 million in revenue, from the amortization of the $67.5 million in upfront and milestone payment earned in 2012 from our collaboration with Merck KGaA. Subsequent to December 31, 2012, we earned an additional $30 million milestone payment. We are amortizing the upfront payment and milestones earned over the period of performance (product development period). We will periodically review and, if necessary, revise the estimated periods of performance of our collaboration.

For the year ended December 31, 2011, we recognized $0.1 million in revenue related to our 2009 agreement with Eleison for the development of glufosfamide, which represents our 50% share of an upfront payment from a sublicense by Eleison. For the year ended December 31, 2010, no revenue was recognized.

We expect revenue to increase in 2013 compared to 2012 due to the full year amortization of milestone payments earned in 2012 as well amortization of additional potential milestone payments we expect to earn in 2013 from our collaboration with Merck KGaA.

Research and Development

Research and development expenses were $18.8 million for the year ended December 31, 2012, compared to $24.4 million for the year ended December 31, 2011. The $5.6 million decrease in expenses is due primarily to a $12.6 million reimbursement for Merck's 70% share of total development expenses for TH-302 and a $0.6 million decrease in consulting expenses, partially offset by $4.1 million increase in clinical development expenses, $2.4 million in employee related expenses and $1.1 million in non-cash stock based compensation.

	Years ended December 31,		
Research and development expenses by project (in thousands)	**2012**	**2011**	**2010**
TH-302	$14,927	$20,692	$16,159
Discovery research	3,859	3,696	2,778
Total research and development expenses	$18,786	$24,388	$18,937

Research and development expenses associated with our internally discovered compound TH-302 were $14.9 million for 2012, which includes the $12.6 million reimbursement for Merck's 70% share of total development expenses for TH-302, $20.7 million for 2011 and $16.2 million for 2010. The decrease of $5.8 in 2012 was due primarily to a $12.6 million reimbursement for Merck's 70% share of total development expenses for TH-302 and $0.5 million decrease in consulting expenses, partially offset by $4.0 million increase in clinical development expenses and $2.5 million in employee related expenses and $0.8 million in non-cash stock based compensation. TH-302 continues to progress through the 406 trial, MAESTRO trial, the 404 trial, and the 403 trial. We reported top-line results for the 404 trial in February 2012 and detailed results in April 2012. We also provided additional overall survival data on the 404 trial in September of 2012.

Discovery research and development expenses were $3.9 million in 2012, $3.7 million for 2011 and $2.8 million for 2010. We continue to focus our efforts towards discovering and developing new drug candidates from our hypoxia activated prodrug platform.

We expect to continue to devote substantial resources to research and development in future periods as we complete our current clinical trials, start additional clinical trials and continue our discovery efforts under our collaboration with Merck as well as on our own. Research and development expenses, including reimbursements of Merck's 70% share of development expenses, are expected to increase in 2013 compared to 2012 due to the continued execution of existing clinical trials and the start of new clinical trials.

General and Administrative

General and administrative expenses were $7.1 million for 2012, compared to $5.7 million for 2011. The $1.4 million increase reflects a $0.9 million increase in non-cash stock compensation expense, $0.7 million in higher consulting expenses and a $0.3 million in higher staffing and facilities expenses. Partially offsetting these increases is a $0.5 million reimbursement of Merck's 70% share of patent expenses and employee expenses related to TH-302 in 2012.

We currently expect our general and administrative expenses to increase in 2013 compared to 2012 due to increased staffing and consulting expenses to support activities related to our collaboration with Merck KGaA and the ongoing development of TH-302.

Interest Income (Expense), Net

Interest income (expense) net for 2012 was $80,000 of interest income compared to $25,000 of net interest income for 2011. The increase in net interest income was primarily due to higher invested balances during 2012 than the prior year.

Other Income (Expense)

Other income (expense) for 2012 was non-cash expense of $51.2 million compared to non-cash income of $4.4 million for 2011. The non-cash expense for 2012 compared to the non-cash income for 2011 was due to a change in the fair value of outstanding warrants to purchase common stock and warrants exercised during 2012 as result of a change in the underlying market price of common stock of the Company. ASC 815 *"Derivatives and Hedging"* requires that stock warrants with certain terms be accounted for as a liability with changes to their fair value recognized in the consolidated statements of operations.

Results of Operations for the Years Ended December 31, 2011 and 2010

Revenue

For the year ended December 31, 2011, we recognized $0.1 million in revenue related to our 2009 agreement with Eleison for the development of glufosfamide, which represents our 50% share of an upfront payment from a sublicense by Eleison. For the year ended December 31, 2010, no revenue was recognized.

Research and Development

Research and development expenses were $24.4 million for the year ended December 31, 2011, compared to $18.9 million for the year ended December 31, 2010. The $5.5 million increase in expenses is due to a $4.8 million increase in clinical and development expenses, $0.4 million in higher staffing expenses and $0.4 million in higher consulting expenses. These increases were partially offset by a $0.2 million decrease in facilities expenses. In addition, stock-based compensation expense increased by $0.1 million.

Research and development expenses associated with our internally discovered compound TH-302 were $20.7 million for 2011and $16.2 million for 2010. The increase of $4.5 million in 2011 was due primarily to an increase in $4.7 million in clinical and manufacturing costs, $0.3 million increase in consulting costs, partially offset by a decrease in employee related expenses of $0.5 million. TH-302 continues to progress through the 406 trial, the 404 trial and the 403 trial. The 403 and 404 trials were expanded and enrollment of patients was completed in the second quarter of 2011. In October 2011, we reported updated top-line results for the 403 trial and we reported top-line results for the 404 trial in February 2012. Enrollment in the 407 trial was completed in the fourth quarter of 2011, and top-line results were presented in the fourth quarter of 2011.

Discovery research and development expenses were $3.7 million in 2011 and $2.8 million for 2010. We continue to focus our efforts towards discovering and developing new drug candidates from our hypoxia activated prodrug platform.

General and Administrative

General and administrative expenses were $5.7 million for 2011, compared to $5.0 million for 2010. The $0.7 million increase reflects a $0.6 million in higher staffing and facilities expenses, as well as a $0.1 million increase in stock-based compensation.

Interest Income (Expense), Net

Interest income (expense) net for 2011 was $25,000 of interest income compared to $60,000 of net interest income for 2010. The decrease in net interest income was primarily due to the lower interest received on investments during 2011 than the prior year.

Other Income (Expense)

Other income (expense) for 2011 was non-cash income of $4.4 million compared to non-cash income of $5.2 million for 2010. The non-cash income for 2011 compared to the non-cash income for 2010 was due to the decrease during 2011 in the fair value of outstanding warrants to purchase 16.6 million shares of common stock warrants. ASC 815 *"Derivatives and Hedging"* requires that stock warrants with certain terms be accounted for as a liability with changes to their fair value recognized in the consolidated statements of operations.

Liquidity and Capital Resources

We have incurred net losses of $323.3 million since inception through December 31, 2012. We have not generated and do not expect to generate revenue from sales of product candidates in the near term. Since our inception, we funded our operations primarily through private placements and public offerings of equity securities and through payments received under our license and co-development agreement with Merck KGaA. During the year ended December 31, 2012, we sold an aggregate of approximately 2.0 million shares of common stock under our at the market stock issuance facility for net proceeds of $12.3 million, and we received approximately $8.8 million from the exercise of warrants to purchase approximately 4.7 million shares of common stock.

During the year ended December 31, 2011 we sold approximately 1.0 million shares of our common stock at an average price of $2.66 under our at the market stock issuance facility, for net proceeds of $2.3 million. In March 2011, we sold to certain investors an aggregate of approximately 14.3 million shares of our common stock for a purchase price equal to $2.05 per share and, for a purchase price equal to $0.05 per share, warrants exercisable for a total of approximately 5.7 million shares of our common stock for aggregate gross proceeds equal to $30.1 million in connection with the offering. The warrants have an exercise price equal to $2.46 per share. Net proceeds generated from the offering were approximately $27.8 million, which includes underwriter discounts and offering costs.

On February 3, 2012, we entered into an agreement with Merck KGaA and to date have received upfront and milestone payments of $97.5 million, including $42.5 million in milestone payments received subsequent to December 31, 2012. We could also receive an additional $12.5 million in a potential milestone payment in 2013. We had cash, cash equivalents and marketable securities of $70.8 million and $20.3 million at December 31, 2012 and December 31, 2011, respectively, available to fund operations.

Net cash provided by operating activities for the year ended December 31, 2012 was $29.9 million compared to net cash used in operating activities for the years ended December 31, 2011 and 2010 was $23.9 million and 22.4 million respectively. The increase of $53.8 million in cash provided by operations in 2012 compared to cash used in operations in 2011 was primarily attributable to $55 million of cash received from upfront and milestone payments related to the Merck KGaA collaboration during year ended December 31, 2012, partially offset by an increase in operating expenses and payments of accrued expenses. The increase of $1.5 million in cash used in operations in 2011 compared to 2010 was primarily attributable to an increase in research and development spending associated with TH-302.

Net cash used in investing activities for the year ended December 31, 2012 was $46.7 million, primarily due to purchases of marketable securities of $93.7 million, offset by proceeds from sales and maturities of investments of $47.6 million. Net cash used in investing activities during the year ended December 31, 2011 was $9.2 million, primarily due to purchases of marketable securities of $28.2 million, offset by maturities of investments of $19.5 million. Net cash provided by investing activities for the year ended December 31, 2010 was $22.1 million, primarily due to proceeds from sales and maturities of marketable securities of $37.4 million, offset by purchases of investments of $15.2 million.

Net cash provided by financing activities was $21.9 million for the year ended December 31, 2012, reflecting $12.3 million received during 2012 primarily as a result of our issuance of common stock under the at the market stock issuance facility, $8.8 million received from the cash exercise of warrants to purchase shares of common stock, and $0.8 million cash received from the issuance of common stock under our equity incentive plans. Net cash provided by financing activities for year ended December 31, 2011 was $30.2 million and primarily due to the approximately $27.8 million of net proceeds from our March 2011 registered direct offering and $2.3 million net proceeds from equity issuances pursuant to our at the market stock issuance facility. Net cash provided by financing activities was $6,000 for the year ended December 31, 2010, due to proceeds from the sale of stock under our equity incentive plans, partially offset by deferred offering costs.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our projected operating requirements for at least the next twelve months based upon current operating plans, milestone payment forecasts and spending assumptions. We may need to raise additional capital to in-license or otherwise acquire and develop additional products or programs.

We may seek to raise capital through a variety of sources, including:

- the public equity market;
- private equity financing;
- collaborative arrangements;
- licensing arrangements; and/or
- public or private debt.

Our ability to raise additional funds will depend on our clinical and regulatory events, our ability to identify promising new in-house development programs or in-licensing opportunities, and factors related to financial, economic, and market conditions, many of which are beyond our control. We cannot be certain that sufficient funds will be available to us when required or on satisfactory terms. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in ownership dilution to our existing stockholders.

In addition, our ability to raise additional capital may be dependent upon our stock being quoted on the NASDAQ Capital Market. If we are unable to secure additional financing on a timely basis or on terms favorable to us, we may be required to cease or reduce certain research and development projects, to sell some or all of our technology or assets or to merge all or a portion of our business with another entity. Insufficient funds may require us to delay, scale back, or eliminate some or all of our activities, and if we are unable to obtain additional funding, there is uncertainty regarding our continued existence.

Obligations and Commitments

We lease certain of our facilities under noncancelable leases, which qualify for operating lease accounting treatment under ASC 840,*"Leases,"* and, as such, these facilities are not included on our consolidated balance sheets. In July 2011, we entered into a noncancelable facility sublease agreement for 28,180 square feet of laboratory space and office space located in South San Francisco, California, which serves as our corporate headquarters. The lease began on October 1, 2011 and will expire on April 30, 2017. The aggregate rent for the term of the lease is approximately $3.4 million. In addition, the lease requires us to pay certain taxes, assessments, fees and other costs associated with the premises, in amounts yet to be determined. We will also be responsible for the costs of certain tenant improvements associated with the leased space. In connection with the execution of the lease we paid a security deposit of approximately $60,000.

Our major outstanding contractual obligations consist of amounts due under our operating lease agreements and purchase commitments under contract research, development and clinical supply agreements. Contractual obligations and related scheduled payments as of December 31, 2012 are as follows (in thousands):

	One to three years (2013 to 2015)	Four to five years (2016 to 2017)	After five years	Total
Facilities leases	$ 1,927	$ 926	$ —	$2,853
Purchase commitments	4,578	—	—	4,578
Total	$ 6,505	$ 926	$ —	$7,431

At the Market Stock Issuance Facility

On October 29, 2010, we entered into an at market issuance sales agreement, or sales agreement, with MLV & Co., LLC, formerly McNicoll, Lewis & Vlak LLC ("MLV"), pursuant to which we were able to issue and sell shares of our common stock having an aggregate offering price of up to $15.0 million from time to time through MLV as our sales agent. Sales of our common stock through MLV will be made on The NASDAQ Capital Market, on any other existing trading market for our common stock, to or through a market maker or as otherwise agreed by MLV and us. Subject to the terms and conditions of the sales agreement, MLV will use commercially reasonable efforts to sell our common stock from time to time, based upon our instructions (including any price, time or size limits or other customary parameters or conditions we may impose). We will pay MLV an aggregate commission rate of 3.0% of the gross proceeds of the sales price per share of any common stock sold under the sales agreement. Under certain circumstances, sales of the stock under the at market issuances sales agreement could result in an adjustment to the exercise price of certain of our outstanding warrants. The number of shares we are able to sell under this arrangement will be limited in practice based on the trading volume of our common stock. As of December 31, 2010 we had not sold any stock pursuant to the sales agreement. For the year ended December 31, 2011, we sold an aggregate of 971,037 shares of our common stock at an average price of $2.66 pursuant to the sales agreement. Net proceeds from the sale of stock in 2011 were $2.3 million. The sales of the stock did not result in an adjustment to the exercise price of certain of our outstanding warrants. Pursuant to an amendment to the at the market issuance sales agreement and a prospectus supplement we filed on January 20, 2012 and pursuant to a new registration statement filed with the Securities and Exchange Commission, we may sell shares of our common stock having an aggregate offering price of up to $15.0 million from time to time through MLV as our sales agent on the terms and conditions described above.

During year ended December 31, 2012, we sold 2,022,144 shares of our common stock at an average price of $6.29 pursuant to the sales agreement. Net proceeds from the sale of stock were $12.3 million. The sale of stock did not result in an adjustment to the exercise price of certain of our outstanding warrants.

License and Development Agreements

On February 3, 2012, we entered into a global license and co-development agreement with Merck KGaA, of Darmstadt, Germany, to co-develop and commercialize TH-302, our small molecule hypoxia-targeted drug. Under the terms of the agreement, Merck will receive co-development rights, exclusive global commercialization rights and will provide us an option to co-commercialize TH-302 in the United States. In exchange, we received an upfront payment of $25 million and received another $72.5 million in development milestones, including $42.5 million subsequent to December 31, 2012. We can earn additional potential milestone payments of $452.5 million, comprised of $112.5 million in regulatory and development milestones and $340 million in sales-based milestones.

In the United States, we will have primary responsibility for development of TH-302 in the soft tissue sarcoma indication. We with Merck KGaA will jointly develop TH-302 in all other cancer indications being pursued. Merck KGaA will pay 70% of worldwide development costs for TH-302. Subject to FDA approval in the United States, Merck KGaA will initially be responsible for commercialization of TH-302 while we will receive a tiered, double-digit royalty on sales. Under the royalty-bearing portion of the agreement, we retain the option to co-promote TH-302 in the United States. Additionally, we retain the option to co-commercialize TH-302 upon the achievement of certain sales or regulatory milestones, allowing us to participate in up to 50% of the profits in the United States depending on total sales. Outside of the United States, Merck KGaA will be solely responsible for the commercialization of TH-302 while we will receive a tiered, double-digit royalty on sales in these territories.

The agreement became effective on March 12, 2012, upon termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. The agreement will continue on a country-by-country basis until the later of the last to expire patent covering TH-302 in such country or ten years following the commercial launch of a product containing TH-302 in such country, unless terminated earlier. Merck has the right to terminate the agreement after the achievement of certain milestones, and each party has the right to terminate the agreement following uncured material breach by the other party.

On October 14, 2009, we entered into an exclusive license agreement with Eleison Pharmaceuticals, Inc. (“Eleison”). Pursuant to the agreement we granted Eleison exclusive worldwide rights to develop and commercialize glufosfamide for the treatment of cancer in humans and animals, and certain other uses. Under the agreement, Eleison is responsible for the development, manufacturing and marketing of glufosfamide. Eleison and Threshold will share equally in the profits of commercialization, if the further clinical development of glufosfamide leads to regulatory approval and marketing.

Eleison will pay us 50% of its profits from commercialization on a quarterly basis, beginning on the date of first commercial sale, if any. Eleison has the right to sublicense some or all of its rights under the agreement, and will pay us 50% of amounts received under any sublicenses, including, without limitation, any royalty payments, license fee payments, milestone payments and payments for any equity or debt purchases by a sublicensee, within 30 days of the receipt of any such amounts or payments by Eleison. Eleison will bear all costs associated with development, commercialization and patent prosecution, and will control product development and commercialization. In addition, Eleison will be responsible for all royalty and milestone payments due under the Baxter license and MediBIC development agreement discussed below. The agreement contemplates that Eleison, to satisfy its diligence obligations, will raise sufficient funds to commence clinical development activities with glufosfamide.

Off-Balance Sheet Arrangements

As of December 31, 2012, 2011 and 2010, 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, 2012, 2011 and 2010 and, accordingly, we did not pay any federal or state income taxes. As of December 31, 2012, we had accumulated approximately $113 million and $110 million in federal and state net operating loss carryforwards, respectively, to reduce future taxable income. If not utilized, our federal and state net operating loss carryforwards begin to expire in 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, 2012, we had research credit carryforwards of approximately $1.7 million and $3.7 million for federal California state income tax purposes, respectively. If not utilized the federal carryforward will expire in 2022. The state research credit carryforward does not have an expiration date.

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 of America. 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.

Revenue Recognition

We recognize revenue in accordance with ASC 605 “Revenue Recognition”, subtopic ASC 605-25 “Revenue with Multiple Element Arrangements” and subtopic ASC 605-28 “Revenue Recognition-Milestone Method”, which provides accounting guidance for revenue recognition for arrangements with multiple deliverables and guidance on defining the milestone and determining when the use of the milestone method of revenue recognition for research and development transactions is appropriate, respectively.

Our 2012 revenues are related to our collaboration arrangement with Merck KGaA, which was entered in February 2012. Our collaboration with Merck provides for various types of payments to us, including non-refundable upfront license, milestone and royalty payments. We recognize revenue when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or

determinable, and collectability is reasonably assured. We will also receive reimbursement for Merck's 70% share for eligible worldwide development expenses for TH-302. Such reimbursement would be reflected as a reduction of operating expenses and not as revenue.

For multiple-element arrangements, each deliverable within a multiple deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. The deliverables under the Merck agreement have been determined to be a single unit of accounting and as such the revenue relating to this unit of accounting will be recorded as deferred revenue and recognized ratably over the term of its estimated performance period under the agreement, which is the product development period. We determine the estimated performance period, and it will be periodically reviewed based on the progress of the related product development plan. The effect of a change made to an estimated performance period and therefore revenue recognized ratably would occur on a prospective basis in the period that the change was made.

Deferred revenue associated with a non-refundable payment received under a collaborative agreement for which the performance obligations are terminated will result in an immediate recognition of any remaining deferred revenue in the period that termination occurred provided that all performance obligations have been satisfied.

We recognize revenue from milestone payments when: (i) the milestone event is substantive and its achievability has substantive uncertainty at the inception of the agreement, and (ii) we do not have ongoing performance obligations related to the achievement of the milestone earned. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment (a) is commensurate with either our performance subsequent to the inception of the arrangement to achieve the milestone or the enhancement of the value of the delivered item or items as a result of a specific outcome resulting from our performance subsequent to the inception of the arrangement to achieve the milestone, (b) relates solely to past performance, and (c) is reasonable relative to all of the deliverables and payment terms (including other potential milestone consideration) within the arrangement. See Note 3, "Collaboration Arrangements", in the Notes to the Consolidated Financial Statements included in part II, Item 8. "Financial Statements and Supplementary Data" on this Annual Report on Form 10-K, for analysis of each milestone event deemed to be substantive or non-substantive.

Determining whether and when some of these revenue recognition criteria have been satisfied often involves assumptions and judgments that can have a significant impact on the timing and amount of revenue we report. Changes in assumptions or judgments or changes to the elements in an arrangement could cause a material increase or decrease in the amount of revenue that we report in a particular period.

Stock-Based Compensation

We account for stock options and stock purchase rights related to our equity incentive plans under the provisions of ASC 718 which requires the recognition of the fair value of stock-based compensation. The fair value of stock options and ESPP shares was estimated using a Black-Scholes option valuation model. This model requires the input of subjective assumptions including expected stock price volatility, expected life and estimated forfeitures of each award. The fair value of equity-based awards is amortized ratably over the requisite service period of the award. Due to the limited amount of historical data available to us, particularly with respect to stock-price volatility, employee exercise patterns and forfeitures, actual results could differ from our assumptions.

We account for equity instruments issued to non-employees in accordance with the provisions of ASC 718 and ASC 505,*"Equity."* As a result, the non-cash charge to operations for non-employee options with service or

other performance criteria is affected each reporting period by changes in the estimated fair value of our common stock, as the underlying equity instruments vest. The two factors which most affect these changes are the price of the common stock underlying stock options for which stock-based compensation is recorded and the volatility of the stock price. If our estimates of the fair value of these equity instruments change, it may have the effect of significantly changing compensation expense.

Fair Value of Warrants

ASC 815 provides guidance that clarifies the determination of whether an instrument (or an embedded feature) is indexed to an entity's own stock, which would qualify for classification as a liability. The guidance requires stock warrants classified as a liability to be fair valued at each reporting period, with the changes in fair value recognized in our consolidated statements of operations. We fair value the warrants using a Black Scholes valuation model. Since the outstanding common stock warrants are fair valued at the end of each reporting period, any change in the underlying assumptions to the Black Scholes valuation model, including the volatility and price of our common stock, may have a significant impact on the expense we recognize related to these common stock warrants.

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 clinical trial 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 or restatement of prior 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 upon the levels of inputs described below, and unrealized gains and losses are included in accumulated other comprehensive income(loss) which is reflected in the consolidated statements of comprehensive loss. 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 statements 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.

We adopted ASC 820, *"Fair Value and Measurements,* in the first quarter of 2008. ASC 820 defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. ASC 820 also establishes a fair value hierarchy which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities. Our short-term investments primarily utilize broker quotes in a non-active market for valuation of these securities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

ASC 820 requires us to maximize the use of observable inputs and minimize the use of unobservable inputs. If a financial instrument uses inputs that fall in different levels of the hierarchy, the instrument will be categorized based upon the lowest level of input that is significant to the fair value calculation. Our financial assets measured at fair value on a recurring basis include securities available for sale. Securities available for sale include money market funds, government securities, commercial paper and corporate debt securities.

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 result in an income tax benefit in the period such determination is made.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT 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 weighted 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 policy also limits the amount we may invest in any one type of investment issuer, thereby reducing credit risk concentrations. 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 increase in the interest rates of one percentage point 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 active pharmaceutical product and some drug 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.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

We have audited the accompanying consolidated balance sheets of Threshold Pharmaceuticals, Inc. as of December 31, 2012 and 2011, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for the two years in the period ended December 31, 2012. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. The consolidated financial statements as of December 31, 2010, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for the year in the year ended December 31, 2010, were audited by other auditors whose report dated March 24, 2011 expressed an unqualified opinion on those statements.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit also 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.

In our opinion, based on our audits and the report of other auditors, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Threshold Pharmaceuticals, Inc., at December 31, 2012 and 2011, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 2012, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Threshold Pharmaceutical, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 7, 2013, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Jose, California
March 7, 2013

Report of Independent Registered Public Accounting Firm

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

In our opinion, the accompanying consolidated statements of operations and comprehensive loss, of stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the results of operations and cash flows of Threshold Pharmaceuticals, Inc. and its subsidiary (the "Company") (a development stage enterprise) for the year ended December 31, 2010, 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.

As discussed in Note 8 to the consolidated financial statements, the Company changed the manner in which it accounts for common stock warrants effective January 1, 2009.

/s/ PricewaterhouseCoopers LLP

San Jose, California
March 24, 2011

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

	December 31, 2012	December 31, 2011
ASSETS		
Current assets:		
Cash and cash equivalents	$ 11,029	$ 5,882
Marketable securities	59,819	14,408
Collaboration receivable	15,635	—
Prepaid expenses and other current assets	1,167	254
Total current assets	87,650	20,544
Property and equipment, net	812	543
Other assets	1,059	1,349
Total assets	$ 89,521	$ 22,436
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 908	$ 2,389
Accrued clinical and development expenses	5,750	4,465
Accrued liabilities	2,257	1,737
Deferred revenue, current	8,536	—
Total current liabilities	17,451	8,591
Warrant liability	32,558	9,209
Deferred revenue, non-current	53,097	—
Deferred rent	268	153
Total liabilities	103,374	17,953
Commitments and contingencies (Note 7)		
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value:		
Authorized: 2,000,000 shares authorized; no shares issued and outstanding.	—	—
Common stock, $0.001 par value:		
Authorized: 150,000,000 shares at December 31, 2012 and 2011; Issued and outstanding: 56,431,207 and 49,128,475 shares at December 31, 2012 and 2011, respectively.	56	49
Additional paid-in capital	309,343	256,563
Accumulated other comprehensive (loss) income	11	(1)
Accumulated deficit	(323,263)	(252,128)
Total stockholders' equity (deficit)	(13,853)	4,483
Total liabilities and stockholders' equity (deficit)	$ 89,521	$ 22,436

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

THRESHOLD PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except per share data)

	Years Ended December 31,		
	2012	2011	2010
Revenue	$ 5,867	$ 62	$ —
Operating expenses:			
Research and development	18,786	24,388	18,937
General and administrative	7,080	5,710	4,971
Total operating expenses	25,866	30,098	23,908
Loss from operations	(19,999)	(30,036)	(23,908)
Interest income (expense), net	80	25	60
Other income (expense), net	(51,216)	4,358	5,166
Net loss	(71,135)	(25,653)	(18,682)
Other comprehensive income (loss):			
Unrealized gain (loss) on available for sale securities	12	(2)	25
Comprehensive loss	$(71,123)	$(25,655)	$(18,657)
Net loss per common share:			
Basic	$ (1.31)	$ (0.56)	$ (0.56)
Diluted	$ (1.31)	$ (0.56)	$ (0.56)
Weighted average number of shares used in per common share calculations:			
Basic	54,219	45,900	33,654
Diluted	54,219	45,900	33,654

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

THRESHOLD PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share and per share data)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balances, December 31, 2009	33,563,670	$ 33	$230,441	$ (24)	$ (207,793)	$ 22,657
Issuance of common stock pursuant to stock plans	138,572	1	139	—	—	140
Stock-based compensation	—	—	803	—	—	803
Change in unrealized gain on marketable securities	—	—	—	25	—	25
Net loss	—	—	—	—	(18,682)	(18,682)
Balances, December 31, 2010	33,702,242	$ 34	$231,383	$ 1	$ (226,475)	$ 4,943
Issuance of common stock to certain investors, net of issuance costs of $2.5 million	15,284,118	15	23,992	—	—	24,007
Issuance of common stock pursuant to stock plans	142,115	—	149	—	—	149
Stock-based compensation	—	—	1,039	—	—	1,039
Change in unrealized gain (loss) on marketable securities	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	(25,653)	(25,653)
Balances, December 31, 2011	49,128,475	$ 49	$256,563	$ (1)	$ (252,128)	$ 4,483
Issuance of common stock to certain investors, net of issuance costs of $0.4 million	2,022,144	2	12,321	—	—	12,323
Exercise of warrants to purchase common stock	4,727,331	5	8,844	—	—	8,849
Issuance of common stock pursuant to stock plans	553,257	—	738	—	—	738
Stock-based compensation	—	—	3,010	—	—	3,010
Reclassification of fair value of warrants exercised from liability to equity	—	—	27,867	—	—	27,867
Change in unrealized gain (loss) on marketable securities	—	—	—	12	—	12
Net loss	—	—	—	—	(71,135)	(71,135)
Balances, December 31, 2012	56,431,207	$ 56	$309,343	$ 11	$ (323,263)	$ (13,853)

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

THRESHOLD PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2012	2011	2010
Cash flows from operating activities:			
Net loss	$(71,135)	$(25,653)	$(18,682)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,008	525	509
Stock-based compensation expense	3,010	1,039	803
Change in common stock warrant value	51,216	(4,358)	(5,166)
(Gain) loss on sale of investments, property and equipment	—	(17)	—
Changes in operating assets and liabilities:			
Collaboration receivable	(15,635)	—	—
Prepaid expenses and other current assets	(623)	(369)	(247)
Accounts payable	(1,481)	2,137	(32)
Accrued clinical and development expenses	1,285	2,026	821
Accrued liabilities	520	914	(149)
Deferred rent	115	(95)	(241)
Deferred revenue	61,633	—	—
Net cash provided by (used in) operating activities	29,913	(23,851)	(22,384)
Cash flows from investing activities:			
Acquisition of property and equipment	(482)	(528)	(108)
Acquisition of marketable securities	(93,745)	(28,154)	(15,223)
Proceeds from sales and maturities of marketable securities	47,551	19,500	37,454
Restricted cash	—	—	12
Net cash provided by (used in) investing activities	(46,676)	(9,182)	22,135
Cash flows from financing activities:			
Proceeds from issuance of common stock and warrants, net of offering expenses	21,910	30,224	140
Deferred offering costs	—	—	(134)
Net cash provided by provided by financing activities	21,910	30,224	6
Net increase (decrease) in cash and cash equivalents	5,147	(2,809)	(243)
Cash and cash equivalents, beginning of period	5,882	8,691	8,934
Cash and cash equivalents, end of period	$ 11,029	$ 5,882	$ 8,691
Non-cash investing and financing activities:			
Change in unrealized gain (loss) in marketable securities	$ 12	$ (2)	$ 25

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

THRESHOLD PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1—SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Description of Operations and Basis of Presentation

Threshold Pharmaceuticals, Inc. (the "Company" or "Threshold") was incorporated in the State of Delaware on October 17, 2001. The Company is a biotechnology company focused on the discovery and development of drugs targeting the severe hypoxia in the microenvironment of solid tumors and the bone marrows of patients with some hematological malignancies. 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, 2012, there has been no financial activity related to this entity.

On February 3, 2012, the Company entered into a global license and co-development agreement with Merck KGaA, of Darmstadt, Germany, to co-develop and commercialize TH-302, the Company's small molecule hypoxia-targeted drug. Under the terms of the agreement, Merck will receive co-development rights, exclusive global commercialization rights and will provide the Company an option to co-commercialize TH-302 in the United States. Primarily as a result of the agreement with Merck, Threshold is no longer considered a Development Stage Company as of the first quarter of 2012. Threshold operates in one business segment.

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.

Liquidity

The Company has a product candidate in various stages of development as well as other candidates in discovery and, since inception, has devoted substantially all of its time and efforts to performing research and development, raising capital and recruiting personnel. The Company has incurred significant losses since its inception. The Company continues to incur substantial expenses related to research and development and management believes that it will continue to do so for the foreseeable future. On February 3, 2012, the Company entered into an agreement with Merck KGaA, which provided for an upfront payment of $25 million. To date, the Company has also received $72.5 million in milestone payments, including $42.5 million in milestone payments received subsequent to December 31, 2012. The Company could also receive an additional $12.5 million in potential milestone payments in 2013. See further details in Note 3, "Collaboration Arrangements".

The Company may raise additional capital or incur indebtedness to fund new in-house development programs or to in-license or otherwise acquire and develop additional products or programs. The Company may seek to raise capital through a variety of sources, including:

- the public equity market;
- private equity financing;
- collaborative arrangements; and/or
- public or private debt.

The Company's ability to raise additional funds will depend on its clinical and regulatory events, its ability to identify promising new in-house development programs or in-licensing opportunities, and factors related to financial, economic, and market conditions, many of which are beyond its control. The Company cannot be certain that sufficient funds will be available when required or on satisfactory terms. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in ownership dilution to existing stockholders. There are no assurances that the Company will be able to raise additional financing on terms acceptable to the Company.

Revenue Recognition

The Company recognizes revenue in accordance with ASC 605 "Revenue Recognition", subtopic ASC 605-25 "Revenue with Multiple Element Arrangements" and subtopic ASC 605-28 "Revenue Recognition-Milestone Method", which provides accounting guidance for revenue recognition for arrangements with multiple deliverables and guidance on defining the milestone and determining when the use of the milestone method of revenue recognition for research and development transactions is appropriate, respectively.

The Company's revenues in 2012 are related to its collaboration arrangement with Merck KGaA, which was entered in February 2012. The collaboration with Merck provides for various types of payments to the Company, including non-refundable upfront license, milestone and royalty payments. The Company recognizes revenue when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable, and collectability is reasonably assured. The Company will also receive reimbursement for Merck's 70% share for eligible worldwide development expenses for TH-302. Such reimbursement is reflected as a reduction of operating expenses and not as revenue.

For multiple-element arrangements, each deliverable within a multiple deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the Company's control. The deliverables under the Merck agreement have been determined to be a single unit of accounting and as such the revenue relating to this unit of accounting will be recorded as deferred revenue and recognized ratably over the term of its estimated performance period under the agreement, which is the product development period. The Company determines the estimated performance period and it will be periodically reviewed based on the progress of the related product development plan. The effect of a change made to an estimated performance period and therefore revenue recognized ratably would occur on a prospective basis in the period that the change was made.

Deferred revenue associated with a non-refundable payment received under a collaborative agreement for which the performance obligations are terminated will result in an immediate recognition of any remaining deferred revenue in the period that termination occurred provided that all performance obligations have been satisfied.

The Company recognizes revenue from milestone payments when: (i) the milestone event is substantive and its achievability has substantive uncertainty at the inception of the agreement, and (ii) the Company does not have ongoing performance obligations related to the achievement of the milestone earned. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment (a) is commensurate with either the Company's performance subsequent to the inception of the arrangement to achieve the milestone or the enhancement of the value of the delivered item or items as a result of a specific outcome resulting from the Company's performance subsequent to the inception of the arrangement to achieve the milestone, (b) relates solely to past performance, and (c) is reasonable relative to all of the deliverables and payment terms (including other potential milestone consideration) within the arrangement. See Note 3, "Collaboration Arrangements," for analysis of milestone events deemed to be substantive or non-substantive.

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 on the date of purchase, to be cash equivalents. All cash and cash equivalents are held in the United States of America in financial institutions or money market funds, which are unrestricted as to withdrawal or use.

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 are reported in net loss, computed using the specific identification cost method. The Company places its marketable securities primarily in U.S. government securities, money market funds, corporate debt securities, commercial paper and certificates of deposit.

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. Estimated fair values for marketable securities, which are separately disclosed in Note 4, are based on market prices for the same or similar instruments. The carrying amount of the common stock warrant liability represents its estimated fair value.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments which potentially subject the Company to concentrations of risk consist principally of cash, cash equivalents and marketable securities. The Company invests in a variety of financial instruments, such as, but not limited to, certificates of deposit, corporate and municipal bonds, United States Treasury and agency securities. 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 by policy, limits the amount of credit exposure with any one financial institution or commercial issuer.

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 one drug candidate in development, which has not 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. Accordingly, leasehold improvements are being amortized over lease terms of approximately 4-6 years. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is reflected in operations.

Impairment of Long-lived assets

In accordance with the provisions of Accounting Standards Codification ("ASC") 360, *"Property, Plant and Equipment,"* 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. 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, 2012, the Company has not incurred any such impairment losses.

Related Parties

The Company's offering of common stock and warrants, on March 16, 2011, included 952,380 shares of common stock and warrants exercisable for a total of 380,952 shares of common stock sold to entities affiliated with Sutter Hill Ventures ("Sutter Hill"). Jeffrey W. Bird, member of the Company's board of directors, is a managing member of Sutter Hill. Also as part of this offering, certain members of the Company's management team purchased 340,472 shares and received warrants to purchase 136,186 shares of common stock.

The Company's offering of common stock and warrants, on October 5, 2009, included 1,570,980 shares of common stock and warrants exercisable for a total of 628,264 shares of common stock sold to entities affiliated with Sutter Hill, and 1,047,120 shares of common stock and warrants exercisable for a total of 418,847 shares of common stock sold to entities affiliated with Three Arch Management III, L.L.C. ("Three Arch"). Jeffrey W. Bird and Wilfred E. Jaeger, members of the Company's board of directors, are managing members of Sutter Hill and Three Arch, respectively. Also as part of this offering, certain members of the Company's management team purchased 248,690 shares and received warrants to purchase 99,475 shares of common stock.

Comprehensive loss

Comprehensive loss is comprised of the Company's net loss and other comprehensive income (loss). Unrealized gain (loss) on available-for-sale marketable securities represents the only component of other comprehensive income (loss).

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

The Company's preclinical and clinical trials are performed by third party contract research organizations (CROs) and/or clinical investigators, 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 of the status of each clinical trial 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.

Bonus Accruals

The Company has bonus programs for eligible employees. Bonuses are determined based on various criteria, including the achievement of corporate, departmental and individual goals. Bonus accruals are estimated based on various factors, including target bonus percentages per level of employee and probability of achieving

the goals upon which bonuses are based. The Company's management periodically reviews the progress made towards the goals under the bonus programs. As bonus accruals are dependent upon management's judgments of the likelihood of achieving the various goals, it is possible for bonus expense to vary significantly in future periods if changes occur in those management estimates.

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 accounts for stock-based compensation in accordance with ASC 718, *"Compensation—Stock Compensation,"* which requires measurement of all employee stock-based compensation awards using a fair-value method and recording of such expense in the consolidated financial statements over the requisite service period. See Note 9 "Equity Incentive Plans and Stock Based Compensation" for further discussion.

The Company accounts for equity instruments issued to non-employees in accordance with the provisions of ASC 718 and ASC 505,*"Equity,"* 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.

NOTE 2—NET LOSS PER COMMON SHARE

Basic net loss per common share is computed by dividing net loss by the weighted-average number of 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 and warrants.

Potential dilutive common shares also include the dilutive effect of the common stock underlying in-the-money stock options and warrants that were calculated based on the average share price for each period using the treasury stock method. Under the treasury stock method, the exercise price of an option or warrant is assumed to be used to repurchase shares in the current period. In addition, the average amount of compensation cost for in-the-money options, if any, for future service that the Company has not yet recognized when the option is exercised, is also assumed to repurchase shares in the current period.

A reconciliation of the numerator and denominator used in the calculation is as follows (in thousands, except per share amounts):

	Years Ended December 31,		
	2012	2011	2010
Numerator:			
Net loss	$(71,135)	$(25,653)	$(18,682)
Denominator:			
Weighted-average number of common shares outstanding	54,219	45,900	33,654
Net loss per share:			
Basic	$ (1.31)	$ (0.56)	$ (0.56)
Diluted	$ (1.31)	$ (0.56)	$ (0.56)

The following warrants, outstanding options, common stock subject to repurchase and purchase rights under the Company's ESPP 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,		
	2012	2011	2010
Shares issuable upon exercise of warrants	11,583	16,643	10,918
Shares issuable upon exercise of stock options	5,099	3,672	2,746
Shares issuable related to the ESPP	79	70	61

NOTE 3—COLLABORATION ARRANGEMENTS

Agreements with Merck KGaA

On February 3, 2012, the Company entered into a global license and co-development agreement with Merck KGaA, of Darmstadt, Germany, to co-develop and commercialize TH-302, the Company's small molecule hypoxia-targeted drug. Under the terms of the agreement, Merck will receive co-development rights, exclusive global commercialization rights and will provide the Company an option to co-commercialize TH-302 in the United States. The Company received an upfront payment of $25 million. To date the Company has also received $72.5 million in milestone payments, including $42.5 million subsequent to December 31, 2012. The milestones earned to date were not deemed to be substantive milestones because the work related to the achievement of these items was predominately completed prior to the inception of the arrangement. The Company is eligible to earn additional potential milestone payments of up to $112.5 million in regulatory and development milestones, including $12.5 million in 2013, and $340 million in commercialization milestones.

In the United States, the Company will have primary responsibility for development of TH-302 in the soft tissue sarcoma indication. The Company and Merck KGaA will jointly develop TH-302 in all other cancer indications being pursued. Merck KGaA will pay 70% of worldwide development expenses for TH-302. Subject to FDA approval in the United States, Merck KGaA will initially be responsible for commercialization of TH-302 with the Company receiving a tiered, double-digit royalty on sales. Under the royalty-bearing portion of the agreement, Threshold retains the option to co-promote TH-302 in the United States. Additionally, the Company retains the option to co-commercialize TH-302, upon the achievement of certain sales and regulatory milestones, allowing the Company to participate in up to 50% of the profits in the United States depending on total sales. Outside of the United States, Merck KGaA will be solely responsible for the commercialization of TH-302 with the Company receiving a tiered, double-digit royalty on sales in these territories. The agreement will continue on a country-by-country basis until the later of the last to expire patent covering TH-302 in such country or ten years following the commercial launch of a product containing TH-302 in such country, unless terminated earlier. Merck has the right to terminate the agreement after the achievement of certain milestones, and each party has the right to terminate the agreement following an uncured material breach by the other party.

The Company's deliverables under the Merck agreement, which include delivery of the rights and license for TH-302 and performance of research and development activities, have been determined to be a single unit of accounting. The delivered license does not have standalone value at the inception of the arrangement due to the Company's proprietary expertise with respect to the licensed compound and related ongoing developmental participation under the global license and co-development agreement, which is required for Merck to fully realize the value from the delivered license. Therefore, the revenue relating to this unit of accounting will be recorded as deferred revenue and recognized over the estimated performance period under the agreement, which is the product development period. The Company recorded the $67.5 million of upfront payment and milestones earned in 2012 as deferred revenue and is amortizing them ratably over its estimated period of performance, which the Company currently estimates to end on March 31, 2020. As a result, the Company recognized $5.9 million of revenue in 2012. The Company will periodically review and, if necessary, revise the estimated periods of performance of our collaboration. The Company also earned a $13.1 million reimbursement for eligible worldwide development expenses for TH-302 from Merck in 2012. Such earned reimbursement has been reflected as a reduction of operating expenses.

Of the remaining potential future milestones, $112.5 million are related to regulatory and development milestones and $340 million are related to commercialization milestones that may be received under the Merck Agreement. Regulatory milestones include the filing and acceptance of regulatory applications for marketing approval in major markets. Development milestones include primarily the initiation of various phases of clinical trials. Commercialization milestones include the achievement of first commercial sales in a particular market or annual product sales in excess of a pre-specified threshold. At the inception of the collaboration agreement the Company assessed regulatory and development milestones to be substantive where there was substantive scientific and regulatory uncertainty of achievement, the amounts of payments assigned were considered to be commensurate with the enhancement of the value of the delivered rights and license of TH-302 and the Company's performance is necessary to the achievement of the milestone. Accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when such milestone is achieved. Regulatory and development milestones that do not meet these conditions were considered non-substantive and payments related to the achievement of such milestones, if any, will be recorded as deferred revenue and amortized ratably over the estimated period of performance. Final determination of whether a development or regulatory milestone is substantive will depend upon the Company's role in achieving the milestone. The specific role and responsibilities related to the regulatory and development activities for certain of these milestones have yet to be determined and may change during the development period. Under the Merck agreement, Merck will initially be responsible for commercialization activities and the Company initially may not be involved in the achievement of these commercialization milestones. These commercialization milestones would typically be achieved after the completion of the Company's regulatory and development activities. The Company would account for the commercialization milestones in the same manner as royalties, with revenue recognized upon achievement of the milestone.

Agreements with Eleison Pharmaceuticals, Inc.

On October 14, 2009, the Company entered into an exclusive license agreement with Eleison Pharmaceuticals, Inc. ("Eleison"). Pursuant to the agreement the Company granted Eleison exclusive worldwide rights to develop and commercialize glufosfamide for the treatment of cancer in humans and animals, and certain other uses. Under the agreement, Eleison is responsible for the development, manufacturing and marketing of glufosfamide. Eleison and the Company will share equally in the profits of commercialization, if the further clinical development of glufosfamide leads to regulatory approval and marketing.

Eleison will pay the Company 50% of its profits from commercialization on a quarterly basis, beginning on the date of first commercial sale, if any. Eleison has the right to sublicense some or all of its rights under the agreement, and will pay the Company 50% of amounts received under any sublicenses, including, without limitation, any royalty payments, license fee payments, milestone payments and payments for any equity or debt purchases by a sublicensee, within 30 days of the receipt of any such amounts or payments by Eleison. Eleison will bear all costs associated with development, commercialization and patent prosecution, and will control product development and commercialization. In addition, Eleison will be responsible for all royalty and milestone payments due under the Baxter license and MediBIC development agreement. The agreement contemplates that Eleison, to satisfy its diligence obligations, will raise sufficient funds to commence clinical development activities with glufosfamide. In 2011, the Company received $0.1 million in revenue, which represents the Company's 50% share of an upfront payment from a sublicense by Eleison.

NOTE 4—FAIR VALUE MEASUREMENTS AND MARKETABLE SECURITIES

The Company accounts for its marketable securities in accordance with ASC 820*"Fair Value Measurements and Disclosures."* ASC 820 defines fair value, establishes a framework for measuring fair value in GAAP, and expands disclosures about fair value measurements. ASC 820 defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. ASC 820 also establishes a fair value hierarchy which requires an entity to maximize the use

of observable inputs and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company utilizes the market approach to measure fair value for its financial assets and liabilities. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets or liabilities. For Level 2 securities that have market prices from multiples sources, a "consensus price" or a weighted average price for each of these securities can be derived from a distribution-curve-based algorithm which includes market prices obtained from a variety of industrial standard data providers (e.g. Bloomberg), security master files from large financial institutions, and other third-party sources. Level 2 securities with short maturities and infrequent secondary market trades are typically priced using mathematical calculations adjusted for observable inputs when available.

The following table sets forth the Company's financial assets (cash equivalents and marketable securities) at fair value on a recurring basis as of December 31, 2012 and 2011:

(in thousands)	Fair Value as of December 31, 2012	Basis of Fair Value Measurements		
		Level 1	Level 2	Level 3
Money market funds	$ 5,886	$ 5,886	$ —	$ —
Certificates of deposit	1,185	—	1,185	—
Corporate debt securities	20,242	—	20,242	—
Government securities	27,899	—	27,899	—
Commercial paper	15,613	—	15,613	—
Total cash equivalents and marketable securities	$ 70,825	$ 5,886	$64,939	$ —

(in thousands)	Fair Value as of December 31, 2011	Basis of Fair Value Measurements		
		Level 1	Level 2	Level 3
Money market funds	$ 4,050	$ 4,050	$ —	$ —
Corporate debt securities	4,690	—	4,690	—
Government securities	5,970	—	5,970	—
Commercial paper	5,548	—	5,548	—
Total cash equivalents and marketable securities	$ 20,258	$ 4,050	$16,208	$ —

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, 2012 and 2011:

As of December 31, 2012 (in thousands):	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
Money market funds	$ 5,886	$ —	$ —	$ 5,886
Certificates of deposit	1,185	—	—	1,185
Corporate debt securities	20,237	6	(1)	20,242
Government securities	27,893	12	(6)	27,899
Commercial paper	15,613	—	—	15,613
	70,814	18	(7)	70,825
Less cash equivalents	(11,006)	—	—	(11,006)
Total marketable securities	$ 59,808	$ 18	$ (7)	$ 59,819

As of December 31, 2011 (in thousands):	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
Money market funds	$ 4,050	$ —	$ —	$ 4,050
Corporate debt securities	4,693	—	(3)	4,690
Government securities	5,968	2	—	5,970
Commercial paper	5,548	—	—	5,548
	20,259	2	(3)	20,258
Less cash equivalents	(5,850)	—	—	(5,850)
Total marketable securities	$14,409	$ 2	$ (3)	$14,408

There were no realized gains or losses in 2012, 2011 and 2010.

As of December 31, 2012, weighted average days to maturity for the Company's available for sale securities was 133 days, with the longest maturity being April 2014.

The following table provides the breakdown of the marketable securities with unrealized losses at December 31, 2012 (in thousands):

As of December 31, 2012 (in thousands):	In loss position for less than twelve months	
	Fair Value	Unrealized Loss
Government securities	$1,118	$ (6)
Corporate debt securities	6,449	(1)
Total marketable securities	$7,567	$ (7)

The Company classifies financial instruments in Level 3 of the fair value hierarchy when there is reliance on at least one significant unobservable input to the valuation model. In addition to these unobservable inputs, the valuation models for Level 3 financial instruments typically also rely on a number of inputs that are readily observable either directly or indirectly. The only Level 3 financial instruments are warrants. The Company determined the fair value of the liability associated with its warrants to purchase 11.6 million shares of outstanding common stock using a Black-Scholes Model. See detailed discussion in Note 8—Stockholders' Equity.

NOTE 5—PROPERTY AND EQUIPMENT

Property and equipment comprise the following (in thousands):

	December 31,	
	2012	2011
Computer and office equipment	$ 436	$ 337
Laboratory equipment	1,593	1,316
Leasehold improvements	523	640
	2,552	2,293
Less: Accumulated depreciation and amortization	(1,740)	(1,750)
Total property and equipment, net	$ 812	$ 543

Depreciation and amortization expense was $0.2 million, $0.2 million and $0.3 million for the years ended December 31, 2012, 2011 and 2010, respectively. In connection with the Company's relocation of its corporate headquarters and laboratories to South San Francisco from Redwood City during 2011, the Company wrote off leasehold improvements and computer and office equipment that were fully depreciated with historical asset values of $2.7 million and $0.6 million, respectively. In addition, the Company incurred leasehold improvements at the new South San Francisco facility of approximately $0.5 million during 2011.

NOTE 6—BALANCE SHEET COMPONENTS

Accrued liabilities comprise the following (in thousands):

	December 31,	
	2012	2011
Payroll and employee related expenses	$2,037	$1,302
Professional services	122	195
Other accrued expenses	98	240
Total accrued liabilities	$2,257	$1,737

NOTE 7—COMMITMENTS AND CONTINGENCIES

The Company leases certain of its facilities under noncancelable leases, which qualify for operating lease accounting treatment under ASC 840,*"Leases,"* and, as such, these facilities are not included on its consolidated balance sheets.

In July 2011, the Company entered into a noncancelable facility sublease agreement for 28,180 square feet of laboratory space and office space located in South San Francisco, California, which will serve as the Company's new corporate headquarters. The lease began on October 1, 2011 and will expire on April 30, 2017. The aggregate rent for the term of the lease is approximately $3.4 million. In addition, the lease requires the Company to pay certain taxes, assessments, fees and other costs associated with the premises, in amounts yet to be determined. The Company will also be responsible for the costs of certain tenant improvements associated with the leased space. In connection with the execution of the lease the Company paid a security deposit of approximately $60,000.

Prior to October 2011, the Company had noncancelable facilities lease and sublease agreements for 67,905 square feet of laboratory and office space for its headquarters in Redwood City, California. The sublease agreement expired on February 28, 2010 and the lease agreement expired on September 30, 2011. The Company also had a noncancelable lease agreement for approximately 6,489 square feet of laboratory space, in Redwood City, California. That lease agreement expired in August 2012.

As of December 31, 2012, the future rental payments required by the Company for all of its facilities under noncancelable operating leases are as follows (in thousands):

Years Ending December 31,	
2013	624
2014	640
2015	663
2016	691
2017	235
Total	$2,853

Rent expense for the years ended December 31, 2012, 2011 and 2010 was $0.7 million, $1.3 million and $1.2 million, respectively.

The Company's purchase commitments at December 31, 2012 were $4.6 million, which are primarily for the manufacture and testing of active pharmaceutical ingredient (API) or drug product for clinical testing.

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 duration of these indemnification agreements is 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. Accordingly, the Company has not recognized any liabilities relating to these agreements as of December 31, 2012.

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—STOCKHOLDERS' EQUITY

Common Stock

On October 29, 2010, the Company entered into an at market issuance sales agreement, or sales agreement, with MLV & Co., LLC, formerly McNicoll, Lewis & Vlak LLC ("MLV"), pursuant to which the Company may issue and sell shares of our common stock having an aggregate offering price of up to $15.0 million from time to time through MLV as sales agent. Subject to the terms and conditions of the sales agreement, MLV will use commercially reasonable efforts to sell the Company's common stock from time to time, based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company will pay MLV an aggregate commission rate of 3.0% of the gross proceeds of the sales price per share of any common stock sold under the sales agreement. Under certain circumstances, sales of the stock under the at market issuances sales agreement could result in an adjustment to the exercise price of certain of our outstanding warrants. In 2010, the Company had not sold any stock pursuant to the sales agreement. In 2011, the Company sold 971,037 shares of its common stock at an average price of $2.66 pursuant to the sales agreement. Net proceeds from the sale of stock were $2.3 million. The sale of stock did not result in an adjustment to the exercise price of certain of its outstanding warrants.

Pursuant to an amendment to the at the market issuance sales agreement and a prospectus supplement the Company filed on January 20, 2012 and pursuant to a new registration statement filed with the Securities and Exchange Commission, the Company may sell shares of its common stock having an aggregate offering price of up to $15.0 million from time to time through MLV as its sales agent. In 2012, the Company sold 2,022,144 shares of our common stock at an average price of $6.29 pursuant to the at market issuance sales agreement. Net proceeds from the sale of stock were $12.3 million. The sale of stock did not result in an adjustment to the exercise price of certain of our outstanding warrants.

On March 16, 2011, the Company sold to certain investors an aggregate of 14,313,081 shares of its common stock for a purchase price equal to $2.05 per share and, for a purchase price of $0.05 per share, warrants exercisable for a total of 5,725,227 shares of its common stock for aggregate gross proceeds equal to $30.1 million in connection with the offering. Net proceeds generated from the offering were approximately $27.8 million which includes underwriter discounts and estimated offering costs. The warrants have a five-year term and an exercise price equal to $2.46 per share of common stock. The number of shares issuable upon exercise of the warrants and the exercise price are subject to adjustment for subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable.

On October 5, 2009, the Company sold to certain investors an aggregate of 18,324,599 shares of its common stock for a purchase price equal to $1.86 per share and, for a purchase price of $0.05 per share, warrants exercisable for a total of 7,329,819 shares of its common stock for aggregate gross proceeds equal to $35.0 million in connection with the offering. Net proceeds generated from the offering were $33.1 million. The warrants have a five-year term and an exercise price equal to $2.23 per share of common stock. The exercise price of the warrants may be adjusted in certain circumstances, including certain issuances of securities at a price equal to less than the then current exercise price. In addition, the number of shares issuable upon exercise of the warrants and the exercise price are subject to adjustment for subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable. As a result of the offering on March 16, 2011, the exercise price of the warrants exercisable for a total of 7,329,819 shares of common stock sold to investors in October 2009 that had an original exercise price of $2.23 per share, was subsequently reduced to $2.05 per share pursuant to the terms of such warrants.

On August 29, 2008, the Company sold to certain investors an aggregate of 8,970,574 shares of its common stock for a purchase price equal to $2.04 per share for aggregate gross proceeds equal to $18.3 million in connection with the offering. Net proceeds generated from the offering were $16.8 million. As part of the sale of common stock, the Company also issued warrants exercisable for a total of 3,588,221 shares of its common stock to the investors. The warrants have a five-year term and an exercise price equal to $2.34 per share of common stock. The exercise price and/or the number of shares of common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including certain issuances of securities at a price equal to less than the then current exercise price, subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable. As a result of the offering on October 5, 2009, the exercise price of the warrants exercisable for a total of 3,588,221 shares of common stock sold to investors in August 2008 that had an original exercise price of $2.34 per share, was subsequently reduced to $1.86 per share pursuant to the terms of such warrants.

Shares Authorized

In May 2010, the Company's stockholder's approved the number of authorized shares of common stock be increased from 50,000,000 to 150,000,000.

Common Stock Warrants

The Company accounts for its common stock warrants under guidance now codified in ASC 815 that clarifies the determination of whether an instrument (or an embedded feature) is indexed to an entity's own stock, which would qualify for classification as liabilities. The guidance required the Company's outstanding warrants to be classified as liabilities and to be fair valued at each reporting period, with the changes in fair value recognized as other income (expense) in the Company's consolidated statements of operations.

In 2012, warrants to purchase 5,060,433 shares of common stock were exercised for net proceeds of approximately $8.8 million. As of the date of exercise of the warrants, the Company transferred the fair value of the warrants of approximately $27.9 million from warrant liability into stockholders' equity in 2012.

At December 31, 2012 and 2011, the Company had warrants outstanding to purchase 3,058,811 and 3,588,221 shares of common stock, respectively, from the August 2008 offering. The fair value of these warrants on December 31, 2012 and 2011 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2012	December 31, 2011
Risk-free interest rate	0.16%	0.25%
Expected life (in years)	0.66	1.66
Dividend yield	—	—
Volatility	118%	84%
Stock price	$ 4.21	$ 1.22

During the years ended December 31, 2012 and 2011, a change in fair value of $9.9 million non-cash expense and $1.1 million non-cash income related to the August 2008 warrants was recorded as other income (expense) in the Company's consolidated statements of operations, respectively.

At December 31, 2012 and 2011, the Company had warrants outstanding to purchase 4,287,940 and 7,329,819 shares of common stock, respectively, from the October 2009 offering. The fair value of these warrants on December 31, 2012 and 2011 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2012	December 31, 2011
Risk-free interest rate	0.25%	0.36%
Expected life (in years)	1.76	2.76
Dividend yield	—	—
Volatility	98%	88%
Stock price	$ 4.21	$ 1.22

During the years ended December 31, 2012 and 2011, a change in fair value of $24.2 million of non-cash expense and $1.4 million of non-cash income related to the October 2009 warrants was recorded as other income (expense) in the Company's consolidated statements of operations, respectively.

At December 31, 2012 and 2011 the Company had warrants outstanding to purchase 4,236,083 and 5,725,227 shares of common stock, respectively, from the March 2011 offering. The fair value of these warrants on December 31, 2012 and 2011, was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2012	December 31, 2011
Risk-free interest rate	0.72%	0.60%
Expected life (in years)	3.21	4.21
Dividend yield	—	—
Volatility	94%	102%
Stock price	$ 4.21	$ 1.22

On March 16, 2011, the Company determined the fair value of the warrants to be $6.1 million and classified that amount of the net proceeds from the March 2011 offering to warrant liability. During the years ended December 31, 2012 and 2011, a change in the fair value of $17.1 million of non-cash expense and $1.9 million of non-cash income related to the March 2011 warrants was recorded as other income (expense) in the Company's consolidated statements of operations, respectively.

The following table sets forth the Company's financial liabilities, related to warrants issued in the August 2008, October 2009 and March 2011 offerings, subject to fair value measurements as of December 31, 2012 and 2011:

(in thousands)	Fair Value as of December 31, 2012	Basis of Fair Value Measurements		
		Level 1	Level 2	Level 3
August 2008 warrants	$ 8,014	$ —	$ —	$ 8,014
October 2009 warrants	11,963	—	—	11,963
March 2011 warrants	12,581	—	—	12,581
Total common stock warrants	$ 32,558	$ —	$ —	$ 32,558

(in thousands)	Fair Value as of December 31, 2011	Basis of Fair Value Measurements		
		Level 1	Level 2	Level 3
August 2008 warrants	$ 1,292	$ —	$ —	$ 1,292
October 2009 warrants	3,738	—	—	3,738
March 2011 warrants	4,179	—	—	4,179
Total common stock warrants	$ 9,209	$ —	$ —	$ 9,209

The following table is a reconciliation of the warrant liability measured at fair value using level 3 inputs (in thousands):

	Warrant Liability
Balance at December 31, 2010	$ 7,499
Issuance of common stock warrants related to March 2011 offering	6,068
Change in fair value of common stock warrants during 2011	(4,358)
Balance at December 31, 2011	$ 9,209
Exercise of common stock warrants during 2012	(27,867)
Change in fair value of common stock warrants during 2012	51,216
Balance at December 31, 2012	$ 32,558

Preferred Share Rights Agreement

On August 8, 2006, the Board of Directors adopted a Preferred Shares Rights Agreement. As part of this agreement, preferred stock purchase rights ("the rights") were distributed to stockholders of record as of August 23, 2006, at the rate of one right for each share of common stock held. The rights become exercisable only upon the acquisition, or the acquisition of the right to acquire, by a person or group of affiliated or associated persons, 15% or more of the outstanding shares of the Company's common stock. Once exercisable, each right entitles the holder to purchase, at a price of $25.00, six one-thousandth of a share of Series A Participating Preferred Stock. For a limited period of time following the announcement of any such acquisition or offer, the rights are redeemable by the Company at a price of $0.01 per right. If the rights are not redeemed or exchanged, each right will then entitle the holder to receive, upon exercise of such right, a number of shares of the Company's common stock having a then current value equal to two times the purchase price of such right. Similarly, if the rights are not redeemed or exchanged and following the acquisition of 15% or more of the outstanding shares of the Company's common stock by a person or group of affiliated or associated persons, (i) the Company consolidates with or merges into another entity, (ii) another entity consolidates with or merges into the Company or (iii) the Company sells or otherwise transfers 50% or more of its consolidated assets or earning power, each right will then entitle the holder to receive, upon exercise of such right, a number of shares of common stock of the acquiring company having a then current value equal to two times the purchase price. For a limited period of time after the exercisability of the rights, each right, at the discretion of the Board of Directors, may be exchanged for one share of common stock per right. The Company has initially reserved 200,000 shares of preferred stock pursuant to the exercise of these rights. These rights expire on August 8, 2016.

Effective July 9, 2008, the Company entered into an amendment (the "First Amendment") to that certain Preferred Shares Rights Agreement, dated as of August 8, 2006, by and between the Company and Mellon Investor Services LLC (the "Rights Agreement"). The First Amendment amended certain terms in the Rights Agreement so that the Company could announce and consummate the 2008 offering of common stock and warrants described above without triggering the Rights Agreement.

Effective September 29, 2009, the Company entered into an additional amendment (the "Second Amendment") to the Rights Agreement. The Second Amendment amended certain terms in the Rights Agreement so that the Company could announce and consummate the 2009 offering described above without triggering the Rights Agreement.

NOTE 9—EQUITY INCENTIVE PLANS AND STOCK BASED COMPENSATION

2004 Equity Incentive Plan

The 2004 Equity Incentive Plan ("2004 Plan"),provides for the granting of incentive stock options, nonstatutory stock options, stock appreciation rights, stock awards and cash awards to employees and consultants. Options granted under the 2004 Plan may be either incentive stock options ("ISOs") or nonqualified stock options ("NSOs"). ISOs may be granted only to Company employees (including officers and directors who are also employees). NSOs may be granted to Company employees and consultants. Stock options may be granted with an exercise price not less than 100% of the fair market value of the common stock on the date of grant. Stock options are generally granted with terms of up to ten years and vest over a period of four years.

On March 1, 2010, the Board of Directors approved an addition of 202,401 shares for issuance under the 2004 Plan effective January 1, 2010. On March 1, 2010 the Board of Directors approved an addition of 2,250,000 shares for issuance under the 2004 Plan and on May 19, 2010 the stockholders of the Company approved the same addition of 2,250,000 shares for issuance under the 2004 Plan. The annual automatic increase to the authorized shares under the 2004 Plan was amended, effective January 1, 2011 to the lesser of:

- 5% of the number of the Company's shares issued and outstanding prior to the preceding December 31;
- 1,250,000 shares;
- an amount determined by the Board of Directors.

Activity under the 2004 Plan is set forth below:

	Shares Available for Grant	Outstanding Options		Weighted Average Exercise Price
		Number of Shares	Exercise Price	
Balances, December 31, 2009	143,505	935,660	$ 0.42–21.66	1.17
Additional shares reserved	2,452,401	—		
Options granted	(1,849,500)	1,849,500	0.99–1.88	1.45
Options exercised	—	(20,000)	0.79–1.30	1.05
Options canceled	19,442	(19,442)	0.79–1.95	1.61
Balances, December 31, 2010	765,848	2,745,718	$ 0.42–3.18	$ 1.36
Additional shares reserved	1,250,000	—		
Options granted	(1,196,500)	1,196,500	1.53–1.86	1.64
Options exercised	—	(11,603)	0.79–1.44	1.24
Options canceled	258,436	(258,436)	0.79–1.88	1.38
Balances, December 31, 2011	1,077,784	3,672,179	$ 0.42–3.18	$ 1.45
Additional shares reserved	1,250,000	—		
Options granted	(1,844,000)	1,844,000	1.38–$7.75	6.24
Options exercised	—	(402,580)	0.79–$3.08	1.39
Options canceled	14,627	(14,627)	0.79–$6.18	4.25
Balances, December 31, 2012	498,411	5,098,972	$ 0.42–$7.75	$ 3.18

At December 31, 2012, stock options outstanding and exercisable by exercise price were as follows:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$0.42 – 1.38	664,316	5.31	$ 1.12	619,876	$ 1.10
$1.44 – 1.44	1,397,189	7.37	1.44	889,657	1.44
$1.49 – 1.62	180,000	8.23	1.58	76,527	1.61
$1.64 – 1.64	962,095	8.41	1.64	378,651	1.64
$1.69 – 6.85	934,372	9.05	4.93	223,131	4.16
$7.00 – 7.75	961,000	9.34	7.28	127,496	7.22
$0.42 – 7.75	5,098,972	8.01	$ 3.18	2,315,388	$ 1.97

The aggregate intrinsic value of options outstanding and options exercisable as of December 31, 2012 were $9.4 million and $5.8 million, respectively. As of December 31, 2012, the ending options vested and expected to vest was 5,050,008 and the aggregate intrinsic value of these options was $9.3 million. The weighted average remaining contractual life and weighted average exercise price of these options were 8 years and $3.16, respectively. The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying awards and the quoted price of the Company's common stock for options that were in-the-money at December 31, 2012.

The total intrinsic value of stock options exercised during the years ended December 31, 2012, 2011 and 2010 were $1.7 million, $6,000 and $15,000, respectively, determined at the date of the option exercise. Cash received from stock option exercises were $0.6 million, $14,000 and $21,000 for the years ended December 31, 2012, 2011 and 2010, respectively. The Company issues new shares of common stock upon exercise of options. In connection with these exercises, there was no tax benefit realized by the Company due to its current loss position.

2004 Employee Stock Purchase Plan

The 2004 Employee Stock 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, 2012, employees had purchased 150,677 shares of common stock under the Purchase Plan at an average price of $1.18. For the year ended December 31, 2011, employees had purchased 130,512 shares of common stock under the Purchase Plan at an average price of $1.03. At December 31, 2012, plan participants had $0.1 million withheld to purchase stock on February 14, 2013, which is included in accrued liabilities on the accompanying consolidated balance sheet. At December 31, 2012, 303,141 shares were authorized and available for issuance under the ESPP.

Stock-based Compensation

The Company recognizes stock-based compensation in accordance with ASC 718, *"Compensation—Stock Compensation."* Under this guidance, stock-based compensation cost is based on the recognition of the grant date fair value estimated in accordance with the provisions of ASC 815 over the service period, which is generally the vesting period. In addition, ASC 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Stock-based compensation expense recognized under ASC 718 in the Company's consolidated statements of operations for the years ended December 31, 2012, 2011 and 2010 related to stock options and ESPP were $3.0 million, $1.0 million and $0.8 million, respectively.

Valuation Assumptions

The Company estimated the fair value of stock options granted using the Black-Scholes option-pricing formula and a single option award approach. This fair value is being amortized ratably over the requisite service periods of the awards, which is generally the vesting period. The fair value of employee stock options and employee purchase rights under the Company's ESPP was estimated using the following weighted-average assumptions for the years ended December 31, 2012, 2011 and 2010:

	Years ended December 31,		
	2012	2011	2010
Employee Stock Options			
Risk-free interest rate	1.12%	1.88%	2.35%
Expected life (in years)	5.99	5.98	5.99
Dividend yield	—	—	—
Volatility	105%	92%	85%
Weighted-average fair value of stock options granted	$5.09	$1.23	$1.05
Employee Stock Purchase Plan			
Risk-free interest rate	0.21%	0.15%	0.40%
Expected life (in years)	1.25	1.25	1.25
Dividend yield	—	—	—
Volatility	111%	80%	88%
Weighted-average fair value of ESPP purchase rights	$3.46	$0.66	$0.80

To determine the expected term of the Company's employee stock options granted, the Company utilized the simplified approach as defined by SEC Staff Accounting Bulletin No. 107, *"Share-Based Payment"*. To determine the risk-free interest rate, the Company utilized an average interest rate based on U.S. Treasury instruments with a term consistent with the expected term of the Company's stock based awards. To determine the expected stock price volatility for the Company's stock based awards, the Company examined historical volatilities for industry peers as well as the Company and utilized a blend of the historical volatilities of the Company and its industry peers. The fair value of all the Company's stock based awards assumes no dividends as the Company does not anticipate paying cash dividends on its common stock.

Employee Stock-based Compensation Expense

Stock-based Compensation Expense As required by ASC 718 the Company recognized $2.8 million, $1.0 million and $0.8 million of stock-based compensation expense related to stock options granted and purchase rights granted under the Company's stock option plans, for the years ended December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012, the total unrecognized compensation cost related to unvested stock-based awards granted to employees under the Company's stock option plans was approximately $8.6 million before estimated forfeitures. This cost will be recorded as compensation expense ratably over the remaining weighted average requisite service period of approximately 2.6 years.

Non-employee Stock-based Compensation Expense

Stock-based compensation expense related to stock options granted to non-employees is recognized ratably, as the stock options are earned. The Company issued options to non-employees, which 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 was 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 ASC 505-50 *Equity-Based Payments to Non-Employees* using the following assumptions:

	Years Ended December 31,		
	2012	2011	2010
Risk-free interest rate	1.93%	1.37%	1.94%
Expected life (in years)	10	5.15	5.00
Dividend yield	—	—	—
Expected volatility	101%	92%	85%

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 $0.2 million, $0.1 million and $37,000 for the years ended December 31, 2012, 2011 and 2010, respectively.

Total stock-based compensation expense was allocated to research and development and general and administrative as follows (in thousands):

	Year Ended December 31,		
	2012	2011	2010
Stock-based compensation expense:			
Research and development	$1,521	$ 471	$381
General and administrative	1,489	568	422
	$3,010	$1,039	$803

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):

	2012	2011	2010
U.S. federal taxes (benefit) at statutory rate	$(24,186)	$ (8,722)	$(6,353)
State federal income tax benefit	(1,160)	(1,995)	(1,593)
Unutilized (utilized) net operating losses	7,455	11,731	9,392
Stock-based compensation	288	223	224
Research and development credits	—	(885)	(732)
Tax assets not benefited	143	1,105	957
Nondeductible warrant expense	17,414	(1,482)	(1,756)
Other	46	25	(139)
Total	$ 0	$ 0	$ 0

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

	December 31,	
	2012	2011
Capitalized start-up costs	$ 209	$ 238
Net operating loss carryforwards	44,769	37,889
Research and development credits	3,513	3,370
Deferred stock compensation	2,115	1,635
Other (accruals, reserves, depreciation)	958	592
Total deferred tax assets	51,564	43,724
Less: Valuation allowance	(51,564)	(43,724)
	$ —	$ —

At December 31, 2012, the Company had federal and state net operating loss carryforwards of approximately $113 million and $110 million, respectively, available to offset future taxable income. The Company's federal and state net operating loss carryforwards will begin to expire in 2021 and 2013, respectively, if not used before such time to offset future taxable income or tax liabilities. For federal and state income tax purposes, a portion of the Company's net operating loss carryforward is subject to certain limitations on annual utilization in case of changes in ownership, as defined by federal and state tax laws. The annual limitation may result in the expiration of the net operating loss before utilization.

The net operating loss deferred tax asset balances as of December 31, 2012 includes $0.4 million of excess tax benefits from stock option exercises. Stockholders' equity (deficit) will be credited if and when such excess tax benefits are ultimately realized.

At December 31, 2012, the Company had federal research and development tax credits of approximately $1.7 million, which expire in the year beginning 2022, and state research and development tax credits of approximately $3.7 million, which 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. The valuation allowance increased by $7.8 million, $11.6 million and by $10.3 million for the years ended December 31, 2012, 2011 and 2010, respectively.

The Company adopted ASC Topic 740-10-50 "*Accounting for Uncertainty of Income Taxes*" ("ASC Topic 740-10-50"), on January 1, 2007. The Company does not believe that its unrecognized tax benefits will change over the next twelve months.

The following table summarizes the activity related to our gross unrecognized tax benefits:

(in thousands)	2012	2011
Gross unrecognized tax benefits at January 1,	$1,100	$1,100
Gross increases (decreases) related to prior year tax positions	—	—
Gross increases (decreases) related to current year tax positions	—	—
Settlements	—	—
Expiration of the statute of limitations for the assessment of taxes	—	—
Gross unrecognized tax benefits at December 31,	$1,100	$1,100

The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2012 and 2011, the Company had no accrued interest or penalties due to the Company's net operating losses available to offset any tax adjustment. The Company currently has no federal or state tax examinations in progress nor has it had any federal or state tax examinations since its inception. As a result of the Company's net operating loss carryforwards, all of its tax years are subject to federal and state tax examination.

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, 2012, the Company has not made any contributions to the 401(k) plan.

NOTE 12—QUARTERLY FINANCIAL DATA (UNAUDITED)

The following table presents certain unaudited quarterly financial information for the eight quarters ended December 31, 2012. This information has been prepared on the same basis as the audited consolidated financial statements and includes all adjustments necessary to state fairly the unaudited quarterly results of operations. Net loss per common share, basic and diluted for the four quarters of each fiscal year, may not sum to the total for the fiscal year because of the different weighted average number of shares outstanding in each of the periods.

2012	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share data)				
Revenue	$ 252	$ 1,797	$1,797	$ 2,021
Net income (loss)	$(115,533)	$17,001	$ (991)	$28,388
Net income (loss) per common share				
Basic	$ (2.30)	$ 0.31	$ (0.02)	$ 0.50
Diluted	$ (2.30)	$ (0.04)	$ (0.06)	$ (0.10)

2011	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share data)				
Revenue	$ —	$ —	$ —	$ 62
Net loss	$(8,330)	$(7,923)	$(4,125)	$(5,275)
Net loss per common share				
Basic	$ (0.23)	$ (0.16)	$ (0.08)	$ (0.11)
Diluted	$ (0.23)	$ (0.16)	$ (0.08)	$ (0.11)

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

We conducted an evaluation as of December 31, 2012, under the supervision and with the participation of our management, including our Chief Executive Officer and Vice President, Finance and Controller, of the effectiveness of the design and operation of our disclosure controls and procedures, which are defined under SEC rules as controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files under the Securities Exchange Act of 1934 (Exchange Act) is recorded, processed, summarized and reported within required time periods and that the information accumulated and communicated to our management, including our Chief Executive Officer and Vice President, Finance and Controller is appropriate, to allow timely decisions, regarding required disclosure. Based upon that evaluation, our Chief Executive Officer and Vice President, Finance and Controller concluded that, as of such date, our disclosure controls and procedures were effective.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) of the Exchange Act. Internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and our Vice President, Finance and Controller, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on criteria established in the *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Management's assessment included evaluation of such elements as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies, and our overall control environment. Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2012.

Our independent registered public accounting firm, Ernst & Young LLP, has audited our internal control over financial reporting as of December 31, 2012. Their attestation report on the audit of our internal control over financial reporting is included below.

Limitations on the Effectiveness of Controls

Our management, including our Chief Executive Officer and Vice President, Finance and Controller, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefit of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of

controls can provide absolute assurance that all control issues and instances of fraud, if any, within Threshold Pharmaceuticals, Inc. have been detected. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Controls over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that occurred during the fourth quarter of the year ended December 31, 2012 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Threshold Pharmaceuticals, Inc.

We have audited Threshold Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Threshold Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Threshold Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Threshold Pharmaceuticals, Inc. as of December 31, 2012 and 2011, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2012 of Threshold Pharmaceuticals, Inc. and our report dated March 7, 2013 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Jose, California
March 7, 2013

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item will be contained in our Proxy Statement for the 2013 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 31, 2012 and is hereby incorporated by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be contained in our Proxy Statement for the 2013 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 31, 2012 and is hereby incorporated by reference.

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

The information required by this item will be contained in our Proxy Statement for the 2012 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 31, 2012 and is hereby incorporated by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item will be contained in our Proxy Statement for the 2012 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 31, 2012 and is hereby incorporated by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item will be contained in our Proxy Statement for the 2012 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 31, 2012 and is hereby incorporated by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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

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

Report of Independent Registered Public Accounting Firm
Consolidated Balance Sheets
Consolidated Statements of Operations and Comprehensive Loss
Consolidated Statements of Stockholders' Equity (Deficit)
Consolidated Statements of Cash Flows
Notes to Consolidated Financial Statements

(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	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.2 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
3.2	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.4 to our Annual Report on Form 10-K filed on March 13, 2009)
3.3	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.3 to our Quarterly Report on Form 10-Q filed on November 4, 2010)
3.4	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
4.1	Certificate of Designations of Rights, Powers and Preferences of Series A Participating Preferred Stock of Registrant (incorporated by reference to Exhibit 3.3 to our Current Report on Form 8-K filed on August 9, 2006)
4.2	Specimen Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
4.3	Amended and Restated Investor Rights Agreement dated November 17, 2003 among the Registrant and the parties listed therein (incorporated by reference to Exhibit 4.3 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
4.4	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 (incorporated by reference to Exhibit 4.4 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
4.5	Preferred Shares Rights Agreement, dated August 8, 2006, by and between Registrant and Mellon Investor Services LLC (incorporated by reference to Exhibit 4.5 to our Current Report on Form 8-K filed on August 9, 2006)
4.6	Form of Rights Certificate (incorporated by reference to Exhibit 4.6 to our Current Report on Form 8-K filed on August 9, 2006)

EXHIBIT NUMBER	DESCRIPTION
4.7	Amendment to Rights Agreement dated July 10, 2008 between the Registrant and Mellon Investor Services LLC (incorporated by reference to Exhibit 4.2 to our Current Report on Form 8-K filed on July 14, 2008)
4.8	Second Amendment to Rights Agreement dated as of September 29, 2009 between the Registrant and Mellon Investor Services LLC (incorporated by reference to Exhibit 4.2 to our Current Report on Form 8-K filed on September 30, 2009)
4.9	Third Amendment to Rights Agreement dated as of March 11, 2011 between the Registrant and Mellon Investor Services LLC (incorporated by reference to Exhibit 4.2 to our Current Report on Form 8-K filed on March 11, 2011)
4.10	Form of Warrant (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed on July 14, 2008)
4.11	Form of Warrant (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed on September 30, 2009)
4.12	Form of Warrant (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed on March 11, 2011)
4.13	Form of Indenture (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-3 filed on June 10, 2011)
10.1+	2001 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
10.2+	2004 Amended and Restated Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to our Annual Report on Form 10-K filed on March 15, 2012)
10.3+	Amended and Restated 2004 Employee Stock Purchase Plan (as amended and restated effective May 22, 2009) (incorporated by reference to Exhibit 99.2 to our Registration Statement on Form S-8 (File No. 333-164865) filed on February 11, 2010)
10.4†	Agreement between the Registrant, Baxter International Inc. and Baxter Oncology GmbH, dated August 5, 2003 (incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
10.5+	Form of Indemnification Agreement by and between the Registrant and its officers and directors (incorporated by reference to Exhibit 10.9 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
10.6†	Development Agreement by and between the Registrant and MediBIC Co. Ltd., dated November 30, 2004 (incorporated by reference to Exhibit 10.14 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004).
10.7	Letter Agreement amending Development Agreement by and between the Registrant and MediBIC Co. Ltd. (incorporated by reference to Exhibit 10.18 to our Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
10.8+	2004 Amended and Restated Equity Incentive Plan (incorporated by reference to Exhibit 10.20 to our Current Report on Form 8-K filed on May 24, 2005)
10.9	Form of Notice of Grant of Stock Options and Stock Option Agreement (incorporated by reference to Exhibit 10.25 to our Current Report on Form 8-K filed on March 17, 2006)
10.10+	Offer Letter by and between the Registrant and Joel A. Fernandes dated November 1, 2007 (incorporated by reference to Exhibit 10.36 to our Current Report on Form 8-K filed on November 2, 2007)

EXHIBIT NUMBER	DESCRIPTION
10.11	Form of Securities Purchase Agreement dated July 9, 2008 (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed on July 14, 2008)
10.12+	Form of Amended and Restated Change of Control Severance Agreement (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed on April 12, 2012)
10.13+	Change of Control Severance Agreement by and between the Registrant and Tillman E. Pearce dated April 9, 2012 (incorporated by reference to Exhibit 10.2 to our Current Report on Form 8-K filed on April 12, 2012)
10.14+	Change of Control Severance Agreement by and between the Registrant and Stewart M. Kroll dated April 9, 2012 (incorporated by reference to Exhibit 10.3 to our Current Report on Form 8-K filed on April 12, 2012)
10.15	Form of Securities Purchase Agreement dated as of September 29, 2009 (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed on September 30, 2009)
10.16†	Exclusive License Agreement dated October 14, 2009 (effective October 5, 2009) by and between the Registrant and Eleison Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.26 to our Annual Report on Form 10-K filed on March 8, 2010)
10.17†	License and Co-Development Agreement between the Registrant and Merck KGaA, dated February 2, 2012 (incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q, filed on August 6, 2012)
10.18	At Market Issuance Sales Agreement by and between the Registrant and McNicoll, Lewis & Vlak LLC dated October 29, 2010 (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed on October 29, 2010)
10.19	First Amendment to the At Market Issuance Sales Agreement by and between the Registrant and MLV & Co., LLC, formerly McNicoll, Lewis & Vlak LLC dated January 20, 2012 (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed on January 20, 2012)
10.20	Sublease by and between the Registrant and Exelixis, Inc. dated as of July 25, 2011 (incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q, filed on November 3, 2011)
23.1*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
23.2*	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, 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, 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
101.INS**	XBRL Instance Document
101.SCH**	XBRL Taxonomy Extension Schema Document
101.CAL**	XBRL Taxonomy Extension Calculation Linkbase Document

EXHIBIT NUMBER	DESCRIPTION
101.DEF**	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB**	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE**	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

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

+ Indicates a management contract or compensatory plan or arrangement.

** This information is deemed furnished and not filed or part of a registration statement or prospectus for purposes of sections 11 or 12 of the Securities Act of 1933, as amended, is deemed not filed for purposes of section 18 of the Securities Exchange Act of 1934, as amended, and otherwise is not subject to liability under these sections.

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 7, 2013

By: /s/ HAROLD E. SELICK, PH.D.
Harold E. Selick, Ph.D.
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 7, 2013
/s/ JOEL A. FERNANDES **Joel A. Fernandes**	Vice President, Finance and Controller (principal financial and accounting officer)	March 7, 2013
/s/ JEFFREY W. BIRD, M.D., PH.D. **Jeffrey W. Bird, M.D., Ph.D.**	Director	March 7, 2013
/s/ BRUCE C. COZADD **Bruce C. Cozadd**	Director	March 7, 2013
/s/ DAVID R. HOFFMANN **David R. Hoffmann**	Director	March 7, 2013
/s/ WILFRED E. JAEGER, M.D. **Wilfred E. Jaeger, M.D.**	Director	March 7, 2013
/s/ GEORGE G. C. PARKER, PH.D. **George G. C. Parker, Ph.D.**	Director	March 7, 2013
/s/ DAVID R. PARKINSON, M.D. **David R. Parkinson, M.D.**	Director	March 7, 2013

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement on Form S-3 (No. 333-174844, No. 333-169689, 333-162719 and 333-153475) and Registration Statement on Form S-8 (No. 333-180149, No. 333-173047, No. 333-167260, No. 333-164865, No. 333-156733, No. 333-126276, No. 333-134598, and No. 333-143130) pertaining to the 2004 Amended and Restated Equity Incentive Plan and Amended and Restated 2004 Employee Stock Purchase Plan of Threshold Pharmaceuticals, Inc. of our reports dated March 7, 2013, with respect to the consolidated financial statements of Threshold Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Threshold Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2012.

/s/ Ernst & Young LLP

San Jose, California
March 7, 2013

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-3 (No. 333-174844, No. 333-169689, 333-162719 and 333-153475) and Registration Statement on Form S-8 (No. 333-180149, No. 333-173047, No. 333-167260, 333-164865, No. 333-156733, No. 333-126276, No. 333-134598, and No. 333-143130) of Threshold Pharmaceuticals, Inc. of our report dated March 24, 2011 relating to the consolidated financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 7, 2013

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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (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 functions):

   (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 7, 2013

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

Exhibit 31.2

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

I, Joel A. Fernandes, 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (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 functions):

   (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 7, 2013

/s/ JOEL A. FERNANDES
Joel A. Fernandes
Vice President, Finance and Controller
(Principal Accounting Officer)

Exhibit 32.1

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, 2012, 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 7, 2013

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

Exhibit 32.2

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, 2012, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Joel A. Fernandes, Vice President, Finance and Controller 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 7, 2013

/s/ Joel A. Fernandes
Joel A. Fernandes
Vice President, Finance and Controller
(Principal Accounting Officer)