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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, 2013

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) of the Act:

Title of Each Class	**Name of Each Exchange On Which Registered**
Common Stock, $0.001 Par Value Per Share	**The NASDAQ Stock Market LLC**
Series A Participating Preferred Stock, $0.001 Par Value Per Share	

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. ☒

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 and non-voting common equity held by non-affiliates of the Registrant based upon the closing price of the Common Stock on the NASDAQ Capital Market on June 30, 2013 was approximately $263,301,745. The calculation of the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant excludes shares of Common Stock held by each officer, director and stockholder that the registrant concluded were affiliates on that date. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

On February 28, 2014 there were 59,345,804 shares of the Registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement for the Registrant's 2014 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the Registrant's fiscal year ended December 31, 2013 are incorporated herein by reference into Part III of this Annual Report on Form 10-K.

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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 or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended or 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 and Merck KGaA's 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 and/or Merck KGaA commence;
- the timing of results of our and Merck KGaA's clinical trials for TH-302;
- our and Merck KGaA's receipt and the timing of regulatory approvals, and our and Merck KGaA's satisfaction of ongoing regulatory review;
- our ability to establish and maintain intellectual property rights for TH-302 and any additional compounds we develop;
- our and Merck KGaA's ability to timely develop a viable commercial formulation of TH-302;
- whether any product candidates that we and/or Merck KGaA are able to commercialize are safer or more effective than other marketed products, treatments or therapies;
- the ability of Eleison Pharmaceuticals Inc., or Eleison, our licensee of glufosfamide, to develop, manufacture, market and otherwise commercialize glufosfamide, and to raise sufficient funds to continue clinical development;
- our and Merck KGaA's research and development activities, including our 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 projected 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 targeted therapeutics 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. 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. 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 may have 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 are investigating TH-302 in the following clinical studies, which are ongoing or recently completed:

Clinical Trial Name	Sponsor	Therapeutic Area	Combination therapy with TH-302	Clinical Stage
TH-CR-406	Threshold	Soft Tissue Sarcoma	doxorubicin	Pivotal Phase 3
MAESTRO	Merck KGaA	Pancreatic Cancer	gemcitabine	Pivotal Phase 3
TH-CR-413	Threshold	Advanced Melanoma	None (TH-302 monotherapy)	Phase 2
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
EMR200592-002	Merck KGaA	Solid tumors and Pancreatic Cancer	None (monotherapy) and with gemcitabine	Phase 1 (Japan)
TH-CR-414	Threshold	Advanced Solid Tumors	None (cardiac safety study)	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 ongoing or recently completed:

Study Sponsor	Therapeutic Area	Combination Therapy with TH-302	Clinical Stage
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 some 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 potential submissions for regulatory approval of TH-302. We will continue to work on broadening the potential 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, which 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. 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. In addition, 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. Tumor hypoxia correlates with poor prognosis in cancer patients and is believed to represent a significant unmet medical need.

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 1,000 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 clinical 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 clinical trials are being conducted under special protocol assessments or SPAs, with the U.S. Food and Drug Administration or FDA. An SPA is a written agreement with the FDA that documents FDA's agreement that the design and planned analysis of a study can adequately address objectives in support of a regulatory submission. However, FDA's determinations for marketing application approval are made after a complete review of a marketing application and are based on the entire data in the application. The FDA and the European Commission have granted TH-302 orphan drug designation for the treatment of soft tissue sarcoma and pancreatic cancer. Initiation of these studies was supported by preclinical data in disease-specific models as well as data from Phase 2 clinical trials in the same patient populations.

In 2013, we also initiated a Phase 2 trial of TH-302 monotherapy in patients with advanced melanoma. 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. Merck KGaA is also conducting an additional Phase 1 trial: a dose-escalation trial of TH-302 as monotherapy and in combination with gemcitabine in Japan.

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. As such, we expect to commence a third registration program in a different solid tumor type in the coming months.

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 an international, randomized, pivotal Phase 3 clinical trial of TH-302 in patients with metastatic or locally advanced unresectable soft tissue sarcoma who have not previously received chemotherapy. The trial, which we refer to as the 406, trial is designed to evaluate the efficacy and safety of TH-302 in combination with doxorubicin, compared to doxorubicin alone. The study is being conducted under an SPA with the FDA. The primary endpoint in the 406 trial is overall survival; secondary 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 Eastern Cooperative Oncology Group or 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 soft tissue sarcoma.

In July 2013, we announced a protocol amendment to the 406 trial. The changes to the protocol included enrollment of 170 additional patients so that the target sample size was increased from 450 patients as originally planned to 620 patients. This increase was intended to adjust for new assumptions about the primary endpoint of overall survival, based on the latest medical findings in soft tissue sarcoma clinical research. Specifically, research in the field suggests that patients who receive standard of care treatment (the same as being used in the control arm of our study) may live longer than has historically been reported. The addition of patients to the 406 trial was required to maintain the statistical power of the study and the ability to detect a clinically meaningful effect of TH-302 with a robust level of statistical significance. The U.S. FDA agreed to the amendment under the existing SPA. In December 2013, we announced that the target enrollment of 620 patients was achieved.

This 406 trial for TH-302 was initiated following results from a multi-center, dose-escalation Phase 1/2 trial of TH-302 in patients with soft tissue sarcoma (which we refer to as 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 soft tissue sarcoma 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/m² were Grade 4 thrombocytopenia and Grade 3 infection with Grade 4 neutropenia. The maximum tolerated dose (MTD) of 300 mg/m² was established for TH-302 in combination with the approved dose of 75 mg/m² doxorubicin with prophylactic growth factor support. Enrollment was expanded at the MTD, and a total of 91 patients with advanced soft tissue sarcoma 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% confidence interval (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 2014: Though we will remain blinded to the data from the ongoing 406 trial, an Independent Data Monitoring Committee, or IDMC, which monitors unblinded patient safety on an ongoing basis, will conduct an interim efficacy and safety analysis after 235 deaths are reported. Current projections suggest that the required number of events may be reached around mid-2014, with the interim analysis to be conducted thereafter. However, because the interim analyse is event-driven, which we do not control, we cannot predict with certainty when the interim analyse will commence. The interim efficacy analysis is designed to allow for the early termination of the study based on achieving a pre-specified improvement in overall survival and the recommendation of the IDMC. Early termination of the study may also result if the IDMC determines that the 406 trial would be unlikely to meet its primary endpoint of overall survival or if unexpected safety events altering the risk-benefit profile are observed. If the IDMC recommends that the study continue as planned, we will remain blinded to the data until the primary analysis of overall survival is conducted, which is scheduled to occur after 434 deaths are reported. We currently project that, unless the IDMC recommends the trial end early, the required number of events may be reached in mid-2015, with the primary analysis of overall survival to be conducted thereafter.

TH-302 program in pancreatic cancer

In December 2012, our partner Merck KGaA opened the global pivotal Phase 3 MAESTRO clinical trial 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.

The MAESTRO trial is a randomized, placebo-controlled, international, multi-center, double-blind Phase 3 clinical 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, overall response rate and disease control rate, as well as assessments of safety and tolerability, pharmacokinetics and biomarkers. The study is being conducted under an SPA with the FDA.

The MAESTRO trial was initiated following results from a randomized, controlled Phase 2b clinical trial of TH-302 in combination with gemcitabine in patients with first-line pancreatic cancer (which we refer to as the 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 U.S. Patients were randomized equally into one of three cohorts: TH-302 at a dose of 240 mg/m² plus gemcitabine (G+T240) or TH-302 at a dose of 340 mg/m² plus gemcitabine (G+T340) 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 (a serum biomarker) response rate as well as various safety parameters.

In February 2012, we announced top-line results that the primary endpoint in the 404 trial was achieved, showing a median progression-free survival of 5.6 months for patients treated with the combination of TH-302 at 240 mg/m^2 and 340 mg/m^2 compared with 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% CI: 0.43 – 0.87), which was highly statistically significant (p=0.005).

Updated results from the 404 trial were reported at the 2012 annual meeting of the American Association of Cancer Research (AACR), the 2012 annual meeting of the European Society of Medical Oncology (ESMO), and, most recently, at the 2013 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO-GI). As presented at ASCO-GI 2013, results from the 404 trial showed a consistent dose effect in terms of improved progression-free survival, increased objective response rate, and decreased CA 19-9 levels in the G+T340 arm compared with the G+T240 and the gemcitabine-alone arms. There was a significant improvement (p=0.008) in progression-free survival associated with 41% reduction of risk for disease progression or death for patients treated with G+T340. This represented a 2.4-month increase in median progression-free survival for patients receiving G+T340 compared with gemcitabine alone. The 12-month overall survival rates were also in favor of the G+T340 treatment group compared with the control arm (38% vs. 26% (p=0.13)). Median overall survival for G, G+T240, and G+T340 was 6.9, 8.7, and 9.2 months, respectively; the differences between treatment groups were not significant, which may be at least partially explained by control arm patients with progressive disease crossing over to one of the G+T treatment arms. In other words, patients receiving gemcitabine alone who crossed over to receive gemcitabine plus TH-302 upon disease progression did contribute to the survival of the control arm. While not statistically significant, the improvement in median overall survival in the gemcitabine plus TH-302 treatment arms was consistent with the improvement in median progression-free survival. The most common adverse events were fatigue, nausea and peripheral edema, and were similar in frequency across treatment groups. Skin and mucosal toxicities, predominantly Grade 1 and 2, and myelosuppression, were the most common adverse events related to TH-302 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. Severe (grade 3/4) myelosuppression was more frequent compared to gemcitabine alone. All other severe adverse events were generally below 10%. There was no significant difference in the percentage of patients discontinuing treatment for adverse events across the three treatment arms.

Development activities planned for 2014: Merck KGaA is responsible for conduct and execution of the MAESTRO trial in patients with pancreatic cancer; enrollment in the trial is ongoing.

TH-302 program in advanced melanoma

In August 2013, we announced the start of a Phase 2 clinical trial to evaluate the efficacy and safety ofTH-302 in patients with melanoma. The study will also investigate a range of biomarkers including serum, tumor biopsy, and PET imaging hypoxia biomarkers that may predict treatment outcomes and be associated with tumor response to TH-302 therapy. The Phase 2 clinical trial is a single-arm, multi-center study investigating the clinical efficacy and safety of TH-302 administered at 480 mg/m2 weekly on a 28-day cycle (three weeks on, one week off) in up to 40 patients with advanced melanoma. The primary endpoint is three-month progression-free survival. Secondary endpoints include response rate, duration of response, overall survival, safety and evaluation of potential imaging, serum, and tissue biomarkers that may be associated with tumor response and predict for efficacy and safety of TH-302 therapy.

Development activities planned for 2014: Enrollment in the trial is ongoing and additional clinical trial sites are being opened.

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. *In 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 vivo* models of multiple myeloma demonstrated that 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 (which we refer to as the 407 trial). The starting dose of TH-302 was 120 mg/m^2 administered daily for 5 days of a 21-day cycle. At the highest dose investigated in this study (550 mg/m^2), two patients developed dose limiting mucosal toxicity. The maximum tolerated daily dose of TH-302 was established at 460 mg/m^2. Early results of this trial suggested activity of TH-302 monotherapy as evidenced by stabilization or reduction of bone marrow and peripheral blast counts in some patients. Thus, a second dosing regimen was evaluated in which TH-302 was administered as a continuous infusion over a 5-day period.

In December 2013, updated results were presented at the 55th Annual Meeting of the American Society of Hematology (ASH). A total of 49 patients with previously treated acute myeloid leukemia, or AML (n=39), acute lymphoblastic leukemia or ALL (n=9) or chronic myeloid leukemia or CML in the blast phase (n=1) initiated therapy with TH-302. In the first part of the trial, a total of 38 patients received 30-minute bolus administration of TH-302 at escalating doses of 120 – 550 mg/m2 (depending on the dose cohort) daily on days 1-5 of a 21-day cycle. In the second part of the trial, a total of 11 patients received TH-302 as a continuous infusion on days 1-5 of a 21-day cycle. Two of three patients treated with continuous infusion of TH-302 (460 mg/m2/day) experienced dose-limiting toxicities of Grade 3 mucositis or Grade 3 hyperbilirubinemia; continuous administration maximum-tolerated dose was established at 330 mg/m2/day.

Generally, a significant rapid cytoreduction was documented early in Cycle 1, but was not maintained prior to initiation of the next cycle. Two AML patients who received 550 mg/m2 bolus TH-302 had complete resolution of leukemia cutis. One AML patient at 550 mg/m2 bolus TH-302 had a complete response with incomplete platelet recovery (CRp), and one AML patient at 440 mg/m2 bolus TH-302 had a complete response.

Development Activities Planned for 2014: Enrollment in the 407 trial is complete, and the trial is in the process of being closed. The responses observed in these very difficult to treat patients are consistent with the monotherapy activity that we have previously observed in a variety of solid tumors. The potential for further evaluation of TH-302 in combination with other chemotherapies for the treatment of advanced leukemias will be assessed.

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 (which we refer to as the 408 trial). The objectives of the 408 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 Velcade® (bortezomib, a proteasome inhibitor currently used to treat patients with multiple myeloma) will be investigated.

The dose of TH-302 administered in the dose escalation portion of the study was 240, 340, or 480 mg/m2 (depending on the dose cohort into which a patient enrolled) given on days 1, 4, 8, and 11 of a 21-day cycle, with 40 mg dexamethasone given on the same days as TH-302. Early results from the dose escalation component of the 408 trial were presented at the ASCO annual meeting in mid-2013 and at the ASH annual meeting in December 2013. As presented at ASH, 14 patients initiated therapy. These patients were heavily pretreated having received 3 to 11 prior treatments (median of 6.5) and all having received a regimen containing bortezomib, an immunomodulatory agent lenalidomide and/or thalidomide, and an alkylating agent. Patients received one to 19 cycles (median of 4 cycles) 3-week cycles of therapy with TH-302 and dexamethasone. No dose-limiting toxicities were reported during Cycle 1 at TH-302 doses of 240 or 340 mg/m2. Two dose-limiting toxicities of Grade 3 stomatitis were reported during Cycle 1 for the two patients treated at 480 mg/m2. Therefore, the maximum tolerated dose was determined to be 340 mg/m2 TH-302. The most frequent Grade 3/4 side effects were thrombocytopenia, leukopenia, anemia, and neutropenia.

Thirteen patients were evaluable for response. Two patients achieved a partial response and 3 patients achieved a minimal response, with the combination of the 2 types of responses comprising a clinical benefit rate of 38 percent. Seven patients had stable disease and one patient had progressive disease. Two patients, one with a partial response and one with stable disease, remained on the study for more than one year (13 to 15 months) before discontinuing. There are few treatment options for patients with advanced multiple myeloma that stop responding to bortezomib and lenalidomide, and responses to subsequent salvage therapy have historically been extremely low. The preliminary results suggest that the combination of TH-302 with dexamethasone is active in some heavily pretreated patients who have failed conventional therapy.

The 408 trial was initially opened at the Dana-Farber Cancer Institute. As announced in December 2013, we have expanded the 408 trial to additional sites to help accelerate enrollment.

Development Activities Planned for 2014: We are currently enrolling patients into the second part of the trial in an effort to better characterize the efficacy and safety of TH-302 at 340 mg/m2 in combination with dexamethasone; we expect to complete enrollment of 15 patients around the middle of 2014. By year-end 2014, we expect to initiate the third part of the trial designed to evaluate the addition of a proteasome inhibitor to the therapeutic regimen.

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. While antiangiogenics have proven to be an important new class of targeted cancer therapy, essentially all tumors eventually become resistant to these treatments. Emerging preclinical research suggests that antiangiogenics may also induce tumor hypoxia. Co-targeting tumor angiogenesis and tumor hypoxia, which is believed to be a key driver of treatment resistance, is one approach to potentially prevent or reverse this mechanism of treatment resistance. 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).
- TH-IST-4003: A Phase 1/2 safety and efficacy study of TH-302 in combination with bevacizumab in patients with recurrent glioblastoma following bevacizumab failure.
- TH-IST-4001: A Phase 1 dose-escalation study of TH-302 in combination with pazopanib in patients with advanced solid tumors.
- TH-IST-4004: A Phase 1/2 study of TH-302 in combination with sorafenib in patients with advanced renal cell carcinoma (RCC) and patients with advanced hepatocellular carcinoma (HCC)

TH-CR-410 Phase 1 Dose Escalation Trial of TH-302 and Sunitinib in Patients with RCC, GIST, and PNET

The 410 trial is evaluating standard full dose sunitinib (50 mg) administered daily (Days 1 – 28 of a 6-week cycle) with TH-302 (240 mg/m2 to 480 mg/m2) administered on days 8, 15 and 22. In 2013, preliminary data from the 410 trial were published online in the ASCO 2013 Annual Meeting Proceedings, and updated preliminary results from 12 patients were reported at the 2013 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. As reported at AACR-NCI-EORTC, no dose-limiting toxicities were observed in the 4 patients treated in the initial cohort at 240 mg/m2. One of 6 evaluable patients treated at 340 mg/m2 had a dose-limiting toxicity of Grade 3 stomatitis. Grade 3 thrombocytopenia and neutropenia were reported in 3 (25%) and 4 (33%) patients, respectively; Grade 4 neutropenia was reported in one patient (8%). Fatigue, nausea, and vomiting were the most common nonhematologic adverse events occurring in 83%, 75%, and 67% of patients, respectively. All cases were grade 1 or 2 except for one report of grade 3 nausea. Partial responses were achieved by one of four (25%) evaluable GIST patients (confirmed) and three of eight (37.5%) evaluable RCC patients (one confirmed). All four patients with partial responses had received prior sunitinib.

Development Activities Planned for 2014: We expect to complete enrollment of additional patients at 480 mg/m2 in the second half of the year to determine the maximum tolerated dose of TH-302 in combination with sunitinib; plans for further investigation of this combination will be assessed.

TH-IST-4003: Phase 1/2 Trial of TH-302 and Bevacizumab in Patients with Glioblastoma Following Bevacizumab Failure

The 4003 trial is evaluating TH-302 in combination with Avastin® (bevacizumab) in patients with recurrent glioblastoma following bevacizumab failure. Chemotherapy with radiotherapy is standard care for newly diagnosed glioblastoma. Bevacizumab is approved in the U.S. for progressive disease following prior therapy. After disease progression on bevacizumab, patients may start a subsequent bevacizumab-containing regimen. These patients typically progress in 5 to 8 weeks.

Preliminary results from the 4003 trial were reported at the ESMO 2012 Congress, and most recently in November 2013 at the 4th Quadrennial World Federation of Neuro-Oncology (WFNO) meeting held in conjunction with the 18th annual 2013 Scientific Meeting and Education Day of the Society for Neuro-Oncology (SNO). No dose-limiting toxicity had been reported at doses of TH-302 up to 670 mg/m2 plus bevacizumab at 10 mg/kg every two weeks. Preliminary data in 14 patients showed one patient achieved a complete response and two patients achieved partial responses according to Response Assessment in Neuro-Oncology (RANO) criteria.

Status: Patients continue to be enrolled in the 670 mg/m2 TH-302 cohort in this investigator-sponsored trial.

TH-IST-4001: Phase 1 Dose Escalation Trial of TH-302 and Pazopanib in Patients with Advanced Solid Tumors

The 4001 trial evaluated TH-302 in combination with pazopanib in patients with advanced solid tumors. Results were reported at the 2013 AACR-NCI-EORTC annual meeting for the 30 patients enrolled with a variety of solid tumors for whom standard therapy or palliative measures were nonexistent or no longer effective. The clinical benefit rate was 76% (n=25 evaluable patients) with three patients with partial responses (12%) and 16 patients with stable disease (64%). The partial responses were observed in patients with neuroendocrine cancer, ovarian cancer, and chondrosarcoma. Treatment-related grade 3 hematological adverse events were reported for neutropenia (7%), thrombocytopenia (7%), and anemia (13%). Treatment-related, grade ³ 2 nonhematologic adverse events included vomiting/nausea/diarrhea (7% grade 3), mucositis (7% grade 3), hand foot syndrome (all grade 2), and hypertension (all grade 2). No grade 4 adverse events have been reported.

Status: The 4001 trial has completed enrollment; plans for further investigation of TH-302 in combination with pazopanib will be assessed

[18F]-HX4 Investigational PET Imaging Agent for Hypoxia

In March 2013, we announced the acquisition of [18F]-HX4 [flortanidazole (18F)] from Siemens Healthcare. [18F]-HX4 is an investigational Positron Emission Tomography (PET) imaging agent for hypoxia developed by Siemens Healthcare Molecular Imaging to potentially identify and quantify the degree of hypoxia in tumors in vivo. PET is a non-invasive nuclear medical imaging technique that produces three-dimensional images of certain functional processes in the entire body or selected organs and tissues. [18F]-HX4 contains a short-lived radioisotope, 18F, which can be detected in a PET scanner. PET imaging is used to help physicians diagnose and treat cancer and is routinely performed in cancer treatment centers globally. [18F]-HX4 has a 2-nitroimidazole “trigger” that is designed to be activated under the extreme hypoxic conditions generally found in tumors but not typically in normal healthy tissue, therefore it will accumulate more in these hypoxic regions. Clinical data has demonstrated the potential of [18F]-HX4 to quantify the degree of hypoxia within different tumors. Threshold initially intends to develop [18F]-HX4 to determine a patient’s tumor hypoxia profile, which may identify patients who will best respond to Threshold’s hypoxia-targeted therapeutics.

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 2014 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	233,000	29,480
Lung cancer	224,210	159,260
Melanoma	76,100	9,710
Kidney and Renal Pelvis	63,920	13,860
Head and Neck	55,070	12,000
Leukemia (all)	52,380	24,090
Pancreatic cancer	46,420	39,590
Liver (& intrahepatic bile duct)	33,190	23,000
Brain (& other nervous system)	23,380	14,320
Myeloma	24,050	11,090
Soft tissue sarcoma (including heart)	12,020	4,740

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 46,000 cases of pancreatic cancer are diagnosed in the U.S. every year. Pancreatic cancer is the twelfth 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 approximately 95% of patients dying from their disease within 5 years. It is estimated that there are around 39,000 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 8%. Two other therapeutic agents have been approved for the first-line treatment of patients with pancreatic cancer. Erlotinib, is approved for the first line of treatment of patients with pancreatic cancer based on its registrational Phase 3 study in combination with gemcitabine shown to convey a median overall survival of 6.4 months and overall response rate (complete plus partial response rate) of 8.6%. Nab-paclitaxel was approved by the FDA as first–line treatment for patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine. Approval was based on an 861-patient Phase 3 clinical trial in chemotherapy-naïve patients with metastatic pancreatic cancer. Nab-paclitaxel plus gemcitabine demonstrated a statistically significant improvement in median overall survival compared to gemcitabine alone (8.5 vs. 6.7 months) (HR 0.72, P<0.0001).

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. or Eleison. Pursuant to the agreement we granted Eleison exclusive worldwide rights to manufacture, 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. We and Eleison will share equally in the profits of commercialization, if the further clinical development of glufosfamide leads to regulatory approval and marketing. We have no further development plans for glufosfamide.

In October 2013, Eleison announced that it had initiated a pivotal Phase 3 clinical trial of glufosfamide for the second-line treatment of patients with pancreatic cancer. According to their corporate news release, this pivotal trial will enroll patients with relapsed or refractory pancreatic cancer following prior chemotherapy treatment. The randomized, open-label trial is being conducted to evaluate the safety and efficacy of glufosfamide, with a target enrollment of 480 patients. The primary endpoint is overall survival with a number of pre-specified secondary endpoints. The trial will exclude insulin-treated diabetic patients. Eleison has an agreement with the FDA on an SPA for this Phase 3 clinical trial. The trial is expected to be completed in 2015.

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. 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 the tumor microenvironment are the design and development of novel hypoxia activated cytotoxic prodrug compounds. 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, for example, 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. TH-302 was our first product candidate from this program and we are pursuing the potential development of other hypoxia activated prodrugs as well as prodrugs activated by other tumor-specific conditions. 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

We do not have our own manufacturing capability for the active pharmaceutical ingredient, or API, or the final drug product of TH-302. Under our license and co-development agreement with Merck KGaA, Merck KGaA has exclusive rights to manufacture TH-302 for clinical and commercial use, except that we have the right to obtain clinical supply of TH-302 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. To date, however, we have relied on, and we expect to continue to rely on, a limited number of third-party single source contract manufacturers and excipient suppliers for the TH-302 API and TH-302 drug product to meet our and Merck KGaA's clinical supply needs of TH-302. We have no long-term commitments or commercial supply agreements with any of our TH-302 suppliers.

While we have developed plans to meet our and Merck KGaA's clinical supply needs for our ongoing clinical trials of TH-302, we base our estimates for the amount of drug product we will need on assumptions about trial enrollment and trial dose levels. If we are not successful in having sufficient quantities of TH-302 API and drug product manufactured, or if manufacturing is interrupted at our single source contract manufacturers for TH-302 API and TH-302 drug product due to regulatory or other reasons, 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. In any event, additional agreements for more supplies of each of our product candidates, including TH-302, will be needed to complete clinical development and/or commercialize them. In this regard, Merck KGaA may need to enter into agreements for additional supplies of TH-302 to commercialize it or develop such capability itself. These products will need to satisfy all cGMP manufacturing requirements, including passing product specifications. Our or Merck KGaA'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 KGaA as applicable, will need to have it manufactured in commercial quantities. It may not be possible to successfully manufacture commercial quantities of TH-302 or increase the manufacturing capacity for TH-302 or any of our other product candidates in a timely or economically feasible manner.

During the years ended December 31, 2013, 2012 and 2011, we spent $29.3 million, $18.8 million and $24.4 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 for TH-302 with Merck KGaA, Darmstadt, Germany, with an option to co-commercialize in the United States. Under the terms of

the agreement, Merck KGaA received co-development rights, exclusive global commercialization rights and provided us an option to co-commercialize TH-302 in the United States. To date we have received upfront and milestone payments of $110 million, including $12.5 million subsequent to December 31, 2013. We can earn additional potential milestone payments of up to $440 million, comprised of $100 million in development and regulatory milestones and $340 million in sales-based milestones.

In the United States, we 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 in the United States, 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 and product by product basis until the later of the last to expire patent covering such product containing 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 KGaA has the right to terminate the agreement on limited notice to us, 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. Pursuant to the agreement we granted Eleison exclusive worldwide rights to manufacture, 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. We and Eleison 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 certain agreements pursuant to which we licensed rights related to glufosfamide. The agreement contemplates that Eleison, to satisfy its diligence obligations, will raise sufficient funds to continue 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 February 26, 2014, we owned 80 U.S. and foreign patents and patent applications relating to TH-302 and its manufacture, formulation and use, each of which are either exclusively (e.g., those related to methods of manufacture or optional sole commercialization rights) or co-exclusively licensed to Merck KGaA. These consisted of 6 issued U.S. patents expiring from 2024 to 2030 and 24 issued foreign patents expiring from 2024 to 2027 (in each case, without including any regulatory-delay based patent term extension), as well as 8 pending U.S., 4 pending Patent Cooperation Treaty and 38 pending foreign national patent applications, which, if issued, would in each case expire from 2024 to 2033 (without including any regulatory- or patent-delay based patent term extension).

Although we have U.S. 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-targeted 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-targeted prodrug product candidates.

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, research 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 or may be 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 is likely to be in highly competitive markets and may eventually compete with other therapies offered by companies who are developing or were developing drugs that target tumor hypoxia. Our competitors may succeed in developing their products before we do, obtaining approvals from the FDA or other regulatory agencies for their products more rapidly than we do, or developing products that are more effective than TH-302. These products or technologies might render our technology obsolete or noncompetitive. There may also be product candidates of which we are not aware at an earlier stage of development that may compete with TH-302.

Our cancer product candidates face competition from established biotechnology and pharmaceutical companies and from generic pharmaceutical manufacturers. In particular, if approved for commercial sale for pancreatic cancer, TH-302 would compete with Gemzar®, marketed by Eli Lilly and Company; Tarceva®, marketed by Genentech and Astellas Oncology; Abraxane® marketed by Celgene; and FOLFIRINOX, which is a combination of generic products that are sold individually by many manufacturers. If approved for sale for soft tissue sarcoma, TH-302 could potentially compete with doxorubicin or the combination of doxorubicin and ifosfamide, generic products sold by many manufacturers.

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, import, export, 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, under cGCPs, that may overlap. Phase 1 clinical 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 approved for commercialization. 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). The cost of preparing and submitting a NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. Under applicable laws and FDA regulations, each NDA submitted for FDA assessment is reviewed for filing 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 goals of reviewing and acting on NDAs within six months of filing for priority NDAs (for drugs addressing serious or life threatening conditions for which there is an unmet medical need) and ten months of filing for standard NDAs. Priority review is assigned by the FDA to drugs that it determines offer major advances in treatment, or provide a treatment where no adequate therapy exists. 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 review of the application the FDA will either issue an approval or a complete response letter outlining the deficiencies in the submission, which may require substantial additional testing or information for the FDA to reconsider the application. 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 postmarketing, or Phase 4 studies, may be made a condition to be satisfied after a drug receives approval. The results of postmarketing 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 an 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 or a major contribution to patient care. 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, conducted or paid for by the sponsor, 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 the Modernization Act, 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, 2013, we had 53 employees, including 17 who hold Ph.D. and/or M.D. degrees. 40 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 reports 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. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this annual report on Form 10-K.

ITEM 1A. RISK FACTORS

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. The risks described below are not the only ones we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Our business could be harmed by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should refer to the other information contained in this annual report on Form 10-K, including our consolidated financial statements and related notes.

Risks Related to Drug Discovery, Development and Commercialization

We are substantially dependent upon the success of TH-302, which is our only product candidate in clinical development. If we and Merck KGaA are unable to successfully develop and obtain regulatory approval for TH-302, our ability to generate revenue from product sales will be significantly delayed.

We have focused our development activities on TH-302, and we do not presently have other compounds in clinical development. Substantially all of our efforts and expenditures over the next few years are expected to be devoted to TH-302. Accordingly, our future prospects are substantially dependent on the successful development, regulatory approval and commercialization of TH-302. In addition, in February 2012, we entered into a global license and co-development agreement for TH-302 with Merck KGaA, with an option to co-commercialize in the United States. The success of this collaboration and the activities of Merck KGaA will significantly impact the development and potential commercialization of TH-302. In addition, TH-302 is not expected to be commercially available in the near term, if at all. Further, the commercial success of TH-302 will depend upon its acceptance by physicians, patients, third party payors and other key decision-makers as a therapeutic and cost-effective alternative to currently available products. If we and Merck KGaA are unable to successfully develop, obtain regulatory approval for and commercialize TH-302, our ability to generate revenue from product sales will be significantly delayed and our business would be materially and adversely affected, and we may not be able to earn sufficient revenues to continue as a going concern.

In addition, the failure of TH-302 to achieve successful clinical trial endpoints, delays in clinical trial enrollment or events or in the clinical development of TH-302 generally, unanticipated adverse side effects related to TH-302 or any other adverse developments or information related to TH-302 would significantly harm our business, our prospects and the value of our common stock. TH-302 is currently the subject of two ongoing pivotal Phase 3 clinical trials being conducted under special protocol assessments, or SPAs, with the U.S. Food and Drug Administration, or FDA: the “406 trial” evaluating TH-302 in combination with doxorubicin versus doxorubicin alone in patients with soft tissue sarcoma, and the MAESTRO trial of TH-302 in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma. There is no guarantee that the results of either of the ongoing Phase 3 clinical trials will be positive. Negative or inconclusive results in either of the Phase 3 clinical trials could cause the FDA to require that we repeat it or conduct additional clinical trials. Even if we believe that the data from required Phase 3 clinical trials is positive, the FDA could require additional trials or other testing before approving TH-302 for marketing. In this regard, the FDA has substantial discretion in the approval process and may refuse to approve any application or decide that our or Merck KGaA’s data is insufficient for approval and require additional preclinical, clinical or other studies. Varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of TH-302. The FDA could also require additional studies or trials to satisfy particular safety concerns noted in our or Merck KGaA’s preclinical or clinical testing. Even if the FDA or other regulatory agency approves TH-302, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing commitments or requirements for post-approval studies, including additional research and development and clinical trials. The FDA and other agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval. We and Merck KGaA will need to obtain regulatory approval from authorities in foreign countries to market our

TH-302 in those countries. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. If we or Merck KGaA fail to obtain approvals from foreign jurisdictions, the geographic market for TH-302 would be limited.

Although we obtained agreement with the FDA on an SPA for our pivotal Phase 3 clinical trial of TH-302 in combination with doxorubicin versus doxorubicin alone in patients with for soft tissue sarcoma and Merck KGaA has obtained agreement with the FDA on an SPA for the pivotal Phase 3 clinical trial of TH-302 in combination with gemcitabine for the treatment of previously untreated locally advanced unresectable or metastatic pancreatic cancer, an agreement on an SPA does not guarantee any particular outcome from regulatory review, including any regulatory approval.

We have obtained an agreement with the FDA on an SPA for the 406 trial of TH-302. Merck KGaA has also obtained an agreement with the FDA on an SPA for the MAESTRO trial of TH-302. 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. Reaching agreement on an SPA is not an indication of approvability. 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. As a result, we do not know how the FDA will interpret the parties' respective commitments under the SPA agreements, how it will interpret the data and results from the 406 trial and the MAESTRO trial, or whether TH-302 will receive any regulatory approvals.

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. Therefore, despite the potential benefits of an SPA agreement, significant uncertainty remains regarding the clinical development of and regulatory approval process for TH-302, and it is possible that we and Merck KGaA might never receive any regulatory approvals for TH-302.

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. A number of companies in the pharmaceutical industry, including us and those with greater resources and experience than us, have suffered significant setbacks in Phase 3 clinical trials, even after encouraging results in earlier clinical trials.

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 in Phase 2 clinical 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 in subsequent larger clinical trials, including in the 406 trial and the MAESTRO trial. In particular, the results that achieved the primary endpoint 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, including in the MAESTRO trial. As a result, despite the results reported in earlier clinical trials for TH-302, we do not know whether the ongoing Phase 3 clinical trials or other clinical trials that we or Merck KGaA may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market TH-302. Our and Merck KGaA's failure to successfully complete clinical trials and obtain regulatory approval for TH-302 would materially and adversely affect our business and our stock price.

We are dependent upon our collaborative relationship with Merck KGaA to further develop, manufacture and commercialize TH-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 for TH-302 with Merck KGaA, Darmstadt, Germany, with an option to co-commercialize in the United States. In the United States, we 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. We have rights to co-promote TH-302 in the United States, which we can exercise by giving notice during specified periods, and have 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 KGaA, including:

- our ability, together with Merck KGaA, to achieve developmental and commercial milestones that will trigger payments to us under the agreement;
- our ability to fund 30% of the global development expenses of TH-302;
- we are not able to control any decisions by Merck KGaA regarding the amount and timing of resource expenditures for the development and commercialization of TH-302;
- Merck KGaA may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial or abandon TH-302, repeat or conduct new clinical trials or require a new formulation of TH-302 for clinical testing;
- possible disagreements with Merck KGaA 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 KGaA 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 KGaA to promote and commercialize TH-302 in foreign countries;
- if TH-302 is approved for commercial sale and we exercise our co-promotion or co-commercialization rights for TH-302 in the United States, if we do not receive timely and accurate information from Merck KGaA regarding sales activities, expenses and resulting operating profits and losses, our estimates at a given point of time could be incorrect and we could be required to record adjustments in future periods or restate our financial results for prior periods;
- loss of significant rights if we fail to meet our obligations under the collaboration agreement;

- Merck KGaA may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- adverse regulatory or legal action against Merck KGaA 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 KGaA, including Merck KGaA's representatives on the joint steering committee or other committees that are administering the agreement;
- Merck KGaA could independently move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors;
- changes in key management personnel at Merck KGaA, including Merck KGaA's representatives on the joint steering committee or other committees that are administering the agreement; and
- possible disagreements with Merck KGaA regarding interpretation or enforcement of the agreement that could result in the delay or termination of the research, development or commercialization of TH-302 or that could result in costly litigation or arbitration that diverts management's attention and resources.

We have limited ability to direct Merck KGaA in its development of TH-302 and we may be unable to obtain any remedy against Merck KGaA if they fail to do so, or do so in a manner that we think is inadequate. Merck KGaA 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 KGaA'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 KGaA. In addition, Merck KGaA 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 KGaA's development and commercial decisions related to TH-302 as well as the extent to which Merck KGaA succeeds in the execution of its strategy. Merck KGaA'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 KGaA must agree on the development plan for TH-302. If we and Merck KGaA cannot agree, clinical trial progress could be significantly delayed. Further, we are required to fund 30% of the global development expenses of TH-302; 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, which could substantially harm our business, financial condition and prospects.

Merck KGaA has the right to terminate the agreement after certain milestones have been met on 90 days' prior written notice, or following our uncured material breach. If Merck KGaA terminates the agreement at its election, 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 KGaA, 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. In turn, this could significantly harm our financial position, adversely affect our stock price and require us to incur all the costs of developing and commercializing TH-302, which are now being largely funded by Merck KGaA. In the future, we may not be able to locate third-party collaborators to develop and market TH-302 and we may lack the capital and resources necessary to develop TH-302 alone.

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

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

Delays the progression of our or Merck KGaA's 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.

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.

In addition, clinical results are susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Negative or inconclusive results or adverse safety events, including patient fatalities that may be attributable to TH-302, during a clinical trial could cause the trial to be terminated or require additional studies. Furthermore, some of our clinical trials are overseen by Independent Data Monitoring Committees, or IDMCs. These independent oversight bodies are comprised of external experts who review the progress of the ongoing clinical trials as well as safety from other trials, and make recommendations concerning a trial's continuation, modification, or termination based on interim, unblinded data. Any of our ongoing clinical trials overseen by an IDMC may be discontinued or amended in response to recommendations made by responsible IDMCs based on their review of such interim trial results and an IDMC may determine to delay or suspend the trial due to safety or futility findings based on events occurring during a clinical trial. For example, as part of our study protocol for the 406 trial, an IDMC monitors patient safety on an ongoing basis and will conduct an interim efficacy and safety analysis after 235 deaths are reported in the trial. If the IDMC at any time determines that data from the 406 trial give rise to safety concerns, the IDMC could recommend that the 406 trial be halted or substantially modified. Moreover, if as a result of the planned interim efficacy analysis for the 406 trial the IDMC determines that the 406 trial would be unlikely to meet its primary endpoint of overall survival, the IDMC could recommend early termination of the 406 trial. The recommended termination of any of our or Merck KGaA's ongoing late-stage clinical trials by an IDMC, including the 406 trial, could materially and adversely impact the future development of TH-302, and our business, prospects, operating results, and financial condition may be materially harmed.

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. Our approach may lead to unintended, or off-target, adverse effects or may lack efficacy or contribution to efficacy in combination with other anti-cancer 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. In this regard, TH-302 may prove to have undesirable or unintended side effects or other characteristics adversely affecting its safety, efficacy or cost effectiveness that could prevent or limit its approval for marketing and successful commercial use, or that could delay or prevent the commencement and/or completion of clinical trials for TH-302.

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

The formulation of TH-302 that we and Merck KGaA 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 suitable for a commercial product. We developed a new formulation of TH-302 that may be suitable for a commercial product, but additional data will be required to verify this and there can be no assurance that we will be able to do so in a timely manner, if at all. If we are not able to develop a viable commercial formulation of TH-302, then we and/or Merck KGaA may be required to repeat some or all of our respective Phase 3 clinical trials of TH-302, or we and Merck KGaA may need to develop an alternative commercial formulation, either of which could delay, perhaps substantially, our ability to obtain any regulatory approvals of TH-302.

Even though we and Merck KGaA have received orphan drug designation for TH-302, we may not receive orphan drug marketing exclusivity for TH-302. Even if we and/or Merck KGaA obtain orphan drug exclusivity, orphan drug exclusivity would afford us and Merck KGaA limited protection, and if another party obtains orphan drug exclusivity for the drugs and indications we are targeting, we may be precluded from commercializing our product candidates in those indications.

We and Merck KGaA have received orphan drug designation for TH-302 for the treatment of soft tissue sarcoma and pancreatic cancer in the United States and the European Union. Under the Orphan Drug Act in the United States, 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. In the EU, orphan drug designation is provided for a drug that is intended to diagnose, prevent or treat a life-threatening or chronically debilitating condition which affects no more than 5 in 10,000 individuals in the EU (approximately 245,000 individuals) and for which no satisfactory method of diagnosis, prevention or treatment of the condition already exists, or if such method does exist, that the orphan product must be of significant benefit to the patient population over existing products. 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 in the US and 10 years for the EU. The orphan drug designation also allows a waiver or reduction in select regulatory fees. 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.

Even if we and Merck KGaA obtain orphan drug exclusivity for TH-302, 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 TH-302 were approved for soft tissue sarcoma and/or pancreatic cancer, other drugs could still be approved for use in treating the same indications covered by TH-302, 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. Although we and Merck KGaA have obtained 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.

Failure to successfully develop and obtain regulatory approval for companion diagnostics could harm our drug development and commercialization strategy.

In March 2013, we announced the acquisition of [18F]-HX4 [flortanidazole (18F)] from Siemens Healthcare. [18F]-HX4 is an investigational radiolabeled hypoxia Positron Emission Tomography tracer developed by Siemens Healthcare Molecular Imaging to potentially identify and quantify the degree of hypoxia in tumors *in vivo*. [18F]-HX4 could potentially be used as a companion diagnostic to hypoxia-targeted therapeutics based on our drug discovery platform. A companion diagnostic is a test or measurement intended to assist physicians in making treatment decisions for their patients. We initially intend to develop [18F]-HX4 to determine a patient's tumor hypoxia profile, which may identify patients who will best respond to our hypoxia-targeted therapeutics. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as [medical devices] and require separate regulatory approval prior to commercialization. We may encounter difficulties in developing and obtaining approval for [18F]-HX4, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation, and we may have difficulties gaining market acceptance of the use of [18F]-HX4 in the clinical or medical community. Because [18F]-HX4 is at an early stage of development, we have yet to seek a meeting with the FDA to discuss our potential [18F]-HX4 companion diagnostic development plans, and therefore cannot yet know what the FDA will require in order to

obtain regulatory approval of [18F]-HX4. In any event, we may not be able to develop or obtain any regulatory approval or clearance for [18F]-HX4, and we may therefore not realize any return on our investment in [18F]-HX4.

We may not develop additional prodrug product candidates suitable for clinical testing, which could limit our growth and revenue potential.

We are focused on the design and development of novel cyotoxic prodrug compounds for the treatment of cancer. However, TH-302 is our only product candidate in clinical development and we may be unable to discover and develop additional product candidates suitable for clinical testing. If we are unable to develop suitable product candidates for clinical testing from our internal efforts, we may pursue additional product candidates through in-licensing. Any growth through in-licensing would depend upon the availability of suitable product candidates at favorable prices and upon advantageous terms and conditions. If we are unable to develop or obtain suitable product candidates, our growth and revenue potential could be significantly harmed.

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.

Even if we obtain regulatory approval for TH-302, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The safety profile of any product will

continue to be closely monitored by the FDA and comparable foreign regulatory authorities after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the label ultimately approved for TH-302, if it achieves marketing approval, may include restrictions on use. Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, or the DOJ, the Office of Inspector General of the Department of Health and Human Services, or HHS, state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved or off-label uses, are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the FDA. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign regulatory authorities. In the United States, engaging in impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which we promote or distribute our drug products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements based on certain sales practices promoting off-label drug uses. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from the Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we are not successful in defending against such actions, those actions could compromise our ability to become profitable.

We do not have a sales force or marketing infrastructure 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, as a company. There are risks involved with establishing our own sales and marketing capabilities, as well as entering into arrangements with third parties to perform these services. Developing an internal sales force and function will require substantial expenditures and will be time-consuming, and we may not be able to effectively recruit, train or retain sales personnel. On the other hand, if we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues will be lower than if we market and sell any products that we develop ourselves. 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 and our financial condition.

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, 2013, we had an operating loss of $26.0 million and a net loss of $28.4 million, including $2.3 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, 2013 was $351.7 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 achievement of certain milestone events under, and the continued effectiveness of, our collaborative arrangement with Merck KGaA;
- the extent of product development funding under our collaborative arrangement with Merck KGaA;
- the terms and timing of any future collaborative, licensing, acquisition or other arrangements that we may establish;
- the scope, rate of progress and cost of our clinical trials and other research and development activities;
- the costs and timing of obtaining regulatory approvals;
- the cost of manufacturing clinical, and establishing commercial, supplies of our product candidates and any products that we may develop;
- the cost and timing of establishing sales, marketing and distribution capabilities;
- 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 our projected operating requirements for at least the next 12 months based upon current operating plans, milestone payment forecasts and spending assumptions. Although 70% of the collaboration expenditures related to development of TH-302 are expected to be funded by Merck KGaA, we expect that we will need to raise additional capital to complete the clinical development of TH-302 and to support new in-house development programs or 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, 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. In addition, our ability to raise additional capital may be dependent upon our common stock remaining listed on the NASDAQ Capital Market. 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, 2013, we had 53 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.

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Our business is increasingly dependent on critical, complex and interdependent information technology systems, including Internet-based systems, to support business processes as well as internal and external communications. The size and complexity of our computer systems make them potentially vulnerable to breakdown, malicious intrusion and computer viruses that may result in the impairment of production and key business processes.

In addition, our systems are potentially vulnerable to data security breaches—whether by employees or others—that may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personal information (including sensitive personal information) of our employees, clinical trial patients, customers and others.

Such disruptions and breaches of security could have a material adverse effect on our business, financial condition and results of operations.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Our prior and potential future equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. If a limitation were to apply, utilization of a portion of our domestic net operating loss and tax credit carryforwards could be limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.

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 facilities 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.

We do not have our own manufacturing capability for TH-302 API or TH-302 drug product. Under our license and co-development agreement with Merck KGaA, Merck KGaA has exclusive rights to manufacture TH-302 for clinical and commercial use, except that we have the right to obtain clinical supply of TH-302 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. To date, however, we have relied on, and we expect to continue to rely on, a limited number of third-party single source contract manufacturers and excipient suppliers for the TH-302 API and TH-302 drug product to meet our and Merck KGaA's clinical supply needs of TH-302. We have no long-term commitments or commercial supply agreements with any of our TH-302 suppliers. 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 manufactured to meet the clinical supply demands for our and Merck KGaA's clinical trials. While we have developed plans to meet our and Merck KGaA's

clinical supply needs for our ongoing clinical trials of TH-302, we base our estimates for the amount of drug product we will need on assumptions about trial enrollment and trial dose levels. If we are not successful in having sufficient quantities of TH-302 API and drug product manufactured, or if manufacturing is interrupted at our single source contract manufacturers and excipient suppliers for TH-302 API and TH-302 drug product due to regulatory or other reasons, 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. In any event, we will need to order additional TH-302 API and drug product and we have in the past experienced delays in the receipt of satisfactory drug product, and any additional delays we may experience in the receipt of satisfactory TH-302 API or drug product could cause significant delays in our clinical trials, which would harm our business. Moreover the need for additional supplies and preparation for registration may require manufacturing process improvements in TH-302 API and drug product. The manufacturing processes improvements 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. Finally, we have not engaged any backup or alternative suppliers for parts of our TH-302 supply chain for our clinical trials. If we are required to engage a backup or alternative supplier, the transfer of technical expertise and manufacturing process to the backup or alternative supplier would be difficult, costly and time-consuming and would increase the likelihood of a significant delay or interruption in manufacturing or a shortage of supply of TH-302.

In any event, additional agreements for more supplies of each of our product candidates, including TH-302, will be needed to complete clinical development and/or commercialize them. In this regard, Merck KGaA may need to enter into agreements for additional supplies of TH-302 to commercialize it or develop such capability itself. We cannot be certain that Merck KGaA can do so on favorable terms, if at all. Merck KGaA will need to satisfy all current good manufacturing practice, or cGMP, regulations, including passing specifications. Merck KGaA's inability to satisfy these requirements could delay our clinical programs and the potential commercialization of TH-302 if approved for commercial sale.

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 KGaA as applicable, will need to have it manufactured in commercial quantities. It may not be possible to successfully manufacture commercial quantities of TH-302 or increase the manufacturing capacity for TH-302 or any of our other product candidates in a timely or economically feasible manner. Prior to commercial launch of TH-302, we may be required to manufacture additional validation batches, which the FDA and other regulatory agencies must review and approve. If we and/or Merck KGaA are unable to successfully manufacture the additional validation batches or increase the manufacturing capacity for TH-302 or any other product candidates, 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 or exportation from such country is interrupted or delayed, 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.

In addition, the TH-302 formulation includes excipients that might be available from a limited number of suppliers. We have not signed long term supply agreements with these excipient suppliers. We or Merck KGaA will need to enter into long term supply agreements to ensure uninterrupted supply of these excipients to continuously manufacture clinical batches or commercial supplies, which we and/or Merck KGaA may be unable to do in a timely or economically feasible manner or at all.

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 single source 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 continue clinical development activities with glufosfamide. Even if Eleison is successful at raising sufficient funding, it may not be successful in developing and commercializing glufosfamide. 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. In such event, since we have no further development plans for glufosfamide, we may not receive any further return on our investment in glufosfamide.

Risks Related to Our Intellectual Property

Hypoxia-targeted 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 U.S. 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-targeted 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-targeted 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. If we are not able to obtain adequate protection for, or defend, the intellectual property position of TH-302 or any other potential future product candidates, then we may not be able to retain or attract collaborators to partner our development programs, including TH-302. Further, even if we can obtain protection for and defend the intellectual property position of TH-302 or any potential future product candidates, we or any of our potential future collaborators still may not be able to exclude competitors from developing or marketing competing drugs. Should this occur, we, Merck KGaA and potential future collaborators may not generate any revenues or profits from TH-302 or any potential future product candidates or our revenue or profit potential would be significantly diminished.

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 and from generic pharmaceutical manufacturers. In particular, if approved for commercial sale for pancreatic cancer, TH-302 would compete with Gemzar®, marketed by Eli Lilly and Company; Tarceva®, marketed by Genentech and Astellas Oncology; Abraxane® marketed by Celgene; and FOLFIRINOX, which is a combination of generic products that are sold individually by many manufacturers. If approved for sale for soft tissue sarcoma, TH-302 could potentially compete with doxorubicin or the combination of doxorubicin and ifosfamide, generic products sold by many manufacturers. There may also be product candidates of which we are not aware at an earlier stage of development that may compete with TH-302 or other product candidates we may develop. In short, each cancer indication for which we are or may be developing products has a number of established medical therapies with which our candidates will compete. Our TH-302 product candidate for targeting the tumor hypoxia is likely to be in highly competitive markets and may eventually compete with other therapies offered by companies who are developing or were developing drugs that target tumor hypoxia.

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.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we would market, sell and distribute our products. As a biotechnology company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Federal healthcare Anti-Kickback Statute will constrain our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. Federal civil and criminal false claims laws and civil monetary penalty laws impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. The federal physician sunshine requirements under the Affordable Care Act requires manufacturers of drugs, devices, biologics and medical supplies to report annually to HHS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations. Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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

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 or Merck KGaA's clinical trials of TH-302;
- announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;
- our or Merck KGaA's failure to meet milestones that would have given rise to payments under our agreement with Merck KGaA;
- announcements by Merck KGaA related to the development of TH-302 or announcements related to our agreement with Merck KGaA;
- adverse actions taken by regulatory agencies with respect to our product candidates, clinical trials, manufacturing processes or sales and marketing activities;
- announcements of clinical trial results by us or our competitors;
- announcements of technological innovations, patents or new products by us or 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 there are large sales of our common stock, the market price of our common stock could drop substantially. In addition, 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.

If our existing stockholders sell a large number of shares of our common stock or the public market perceives that existing stockholders might sell shares of our common stock, the market price of our common stock could decline significantly. As of February 28, 2014, we had 59,345,804 outstanding shares of common stock, substantially all of which may be sold in the public market without restriction. In addition, a significant number of shares of our common stock are subject to issuance upon the exercise outstanding warrants. 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. As of December 31, 2013, warrants to purchase 1,731,444 shares of common stock issued in March 2011 and warrants to purchase 3,041,879 shares of common stock issued in October 2009 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, with MLV & Co., LLC), 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 how many of these remaining warrants will ultimately be exercised, the warrants will likely 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.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 could have a material adverse effect on our stock price.

Section 404 of the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the Securities and Exchange Commission, or SEC, require annual management assessments of the effectiveness of our internal

control over financial reporting and a report by our independent registered public accounting firm attesting to, and reporting on, the effectiveness of our internal control over financial reporting. If we fail to maintain the adequacy of our internal control over financial reporting, as such standards are modified, supplemented or amended from time to time, we may not be able to ensure that we can conclude on an ongoing basis that we have effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the SEC. If we cannot favorably assess, or our independent registered public accounting firm is unable to provide an unqualified attestation report on, the effectiveness of our internal control over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on our stock price.

Our certificate of incorporation, our bylaws, our preferred shares rights agreement 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, or the rights plan, 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. The rights plan could also reduce the price that investors might be willing to pay for shares of our common stock and result in the market price being lower than it would be without the rights plan. In addition, the existence of the rights plan itself may deter a potential acquiror from acquiring us. As a result, either by operation of the rights plan or by its potential deterrent effect, mergers and acquisitions of us that our stockholders may consider in their best interests may not occur.

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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We have a noncancelable facility sublease agreement for 28,650 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. In November 2013, we entered into a noncancelable facility lease agreement for 7,934 square feet for additional office space located in South San Francisco, California. The lease began on December 1, 2013 and will expire on December 31, 2016. 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

We are not a party to any material legal proceedings.

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

Market Information

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 for the periods indicated below.

	High	Low
Year Ended December 31, 2013:		
First Quarter	$5.54	$4.15
Second Quarter	$6.11	$4.20
Third Quarter	$6.05	$4.30
Fourth Quarter	$5.23	$4.02
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

There were approximately 79 holders of record of our common stock as of February 28, 2014.

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.

Unregistered Sales of Equity Securities

From January 1, 2013 through December 31, 2013, we issued an aggregate of 691,175 shares of our common stock pursuant to the cash exercise of warrants that were originally issued to the investors in our August 2008 private placement, which private placement was previously reported by us on a current report on Form 8-K. These warrants, which were exercised for cash, had an exercise price of $1.86 per share, resulting in aggregate cash consideration to us of $1.3 million.

In addition to the cash warrant exercises reported above, from January 1, 2013 through December 31, 2013, we issued an aggregate of 1,555,043 shares of our common stock pursuant to the net, or cashless, exercise of warrants that were originally issued to the investors in our August 2008 private placement. These warrants were exercisable for an aggregate of 2,367,636 shares of common stock and had an exercise price of $1.86 per share. The number of shares issued upon the exercise of these warrants was reduced by an aggregate of 812,593 shares to effect the net exercise of the warrants in accordance with their terms.

In issuing the above-mentioned shares, we relied on the exemptions provided by (i) Section 4(a)(2) of the Securities Act and/or Regulation D promulgated thereunder as a transaction by an issuer not involving a public offering or (ii) Section 3(a)(9) of the Securities Act of 1933, as applicable.

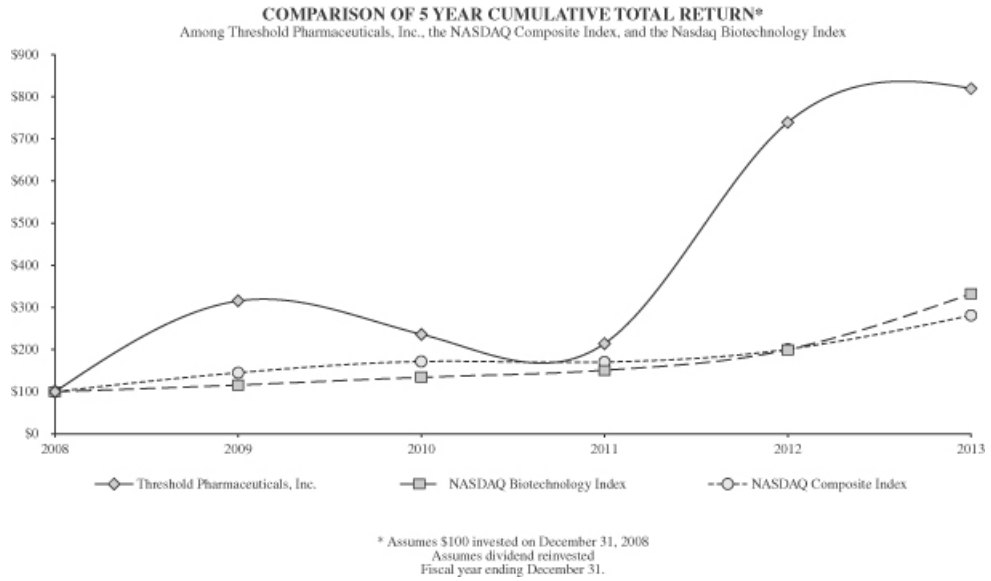
Repurchases of Equity Securities

None.

Stock Performance Graph

The following graph shows the total stockholder return of an investment of $100 in cash on December 31, 2008 for (i) our common stock; (ii) the NASDAQ Composite Index; and (iii) the NASDAQ Biotechnology Index through December 31, 2013. Pursuant to applicable SEC 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 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.

	Years Ended December 31,				
	2013	2012	2011	2010	2009
	(In thousands, except per share data)				
Revenue	$ 12,495	$ 5,867	$ 62	$ —	$ —
Operating expenses:					
Research and development (1)	29,334	18,786	24,388	18,937	15,844
General and administrative (1)	9,185	7,080	5,710	4,971	5,480
Total operating expenses	38,519	25,866	30,098	23,908	21,324
Loss from operations	(26,024)	(19,999)	(30,036)	(23,908)	(21,324)
Interest income (expense), net	136	80	25	60	(13)
Other income (expense), net	(2,325)	(51,216)	4,358	5,166	(2,311)
Income (loss) before provision for income taxes	(28,213)	(71,135)	(25,653)	(18,682)	(23,648)
Provision for income taxes	202	—	—	—	—
Net loss	$ (28,415)	$ (71,135)	$ (25,653)	$ (18,682)	$ (23,648)
Net loss per common share:					
Basic and diluted	$ (0.49)	$ (1.31)	$ (0.56)	$ (0.56)	$ (1.21)
Weighted average number of shares used in net loss per common share calculations:					
Basic and diluted	57,832	54,219	45, 900	33,654	19,594
(1) Includes employee and non-employee non-cash stock-based compensation of:					
Research and development	$ 2,562	$ 1,521	$ 471	$ 381	$ 1,003
General and administrative	$ 2,360	$ 1,489	$ 568	$ 422	$ 1,208

	As of December 31,				
	2013	2012	2011	2010	2009
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 82,033	$ 70,848	$20,290	$14,699	$37,315
Working capital	58,993	70,199	11,953	12,129	34,783
Total assets	104,118	89,521	22,436	16,204	48,685
Total liabilities	127,593	103,374	17,953	11,261	26,028
Total stockholders' equity (deficit)	(23,475)	(13,853)	4,483	4,943	22,657

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-targeted therapeutics 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. 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. 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 may have 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.

The most advanced clinical study of TH-302 is a pivotal Phase 3 clinical trial of TH-302 plus doxorubicin versus doxorubicin alone in patients with soft tissue sarcoma, which we refer to as the 406 trial. In July 2013, we announced protocol changes to the 406 trial, including an increase in target enrollment from 450 to 620 patients; enrollment of 620 patients was completed in December 2013. An interim efficacy and safety analysis is expected to be conducted by an Independent Data Monitoring Committee after 235 deaths are reported. The timing of reaching the number of events, which is dependent on the length of survival of patients, is currently projected to be in mid-2014, with the analysis to be conducted thereafter. However, because the interim analysis is event-driven, which we do not control, we cannot predict with certainty when the interim analysis will commence. In January 2013, we announced that our partner Merck KGaA initiated the global Phase 3 MAESTRO (**M**etast**A**tic or unr**ES**ectable pancrea**T**ic adenoca**R**cin**O**ma) 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. Initiation of the pivotal Phase 3 MAESTRO clinical trial followed completion of our randomized and controlled Phase 2 clinical trial of TH-302 plus gemcitabine in patients with pancreatic cancer (which we refer to as the 404 trial) in which the primary endpoint of progression-free survival was met. We also expect to commence a third registration program in a different solid tumor type in the coming months.

In August 2013, we announced the initiation of a Phase 2 clinical trial of TH-302 as single-agent monotherapy in patients with advanced melanoma (which we refer to as the 413 trial). 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 leukemias (which we refer to as the 407 trial). The 407 trial is closed to enrollment and results were reported at the annual meeting of the American Society of Hematology or ASH in December 2013. 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 (which we refer to as the 408 trial). Initial results from the dose escalation portion of the 408 trial were reported at the annual meeting of the American Society of Clinical Oncology or ASCO in June 2013, and updated results were reported at the December 2013 ASH annual meeting showing initial signs of clinical activity of the combination of TH-302 and dexamethasone in heavily pretreated relapsed/refractory multiple myeloma patients. The maximum tolerated dose was established at 340 mg/m^2 TH-302 and enrollment of additional patients at the maximum tolerated dose is ongoing.

TH-302 is the subject of four clinical trials investigating the combination of TH-302 with antiangiogenic therapies in a variety of tumor types. Threshold is the sponsor of a Phase 1 dose-escalation study of TH-302 in combination with sunitinib in patients with advanced renal cell carcinoma or RCC, gastrointestinal stromal tumors or GIST, and pancreatic neuroendocrine tumors or PNET (which we refer to as the 410 trial). In October 2013, interim results were reported at the AACR-NCI-EORTC 2013 Molecular Targets and Cancer Therapeutics meeting on the first twelve patients demonstrating that one of four patients with GIST achieved a confirmed PR, and three of eight patients with RCC achieved PRs; enrollment continues. Investigator sponsored trials of TH-302 administered in combination with antiangiogenics include: a Phase 1/2 randomized study of TH-302 in combination with bevacizumab in recurrent glioblastoma following bevacizumab failure; a Phase 1 dose-escalation study of TH-302 in combination with pazopanib in advanced solid tumors; and a Phase 1/2 study of TH-302 in combination with sorafenib in advanced RCC and advanced hepatocellular carcinoma. Initial results from a small number of patients with glioblastoma were reported at the European Society for Medical Oncology (ESMO) 2012 Congress, and an update was given at the World Federation of Neuro-oncology meeting in November 2013 demonstrating initial signs of clinical activity of TH-302 plus bevacizumab in some patients. The study continues to enroll patients. Results in patients with advanced solid tumors were reported at AACR-NCI-EORTC showing that patients treated with the combination of pazopanib and TH-302 (n=30) achieved a clinical benefit rate of 76% (partial response rate of 12% plus stable disease rate of 64%). The study has completed enrollment and treatment is ongoing.

We are working to broaden the potential applicability of TH-302 to other cancers and in combination with other approved anti-cancer drugs as well as to discover additional hypoxia-targeted therapeutics that will selectively target cancer cells. We also seek to improve our capability of identifying patients who may be most likely to respond to our hypoxia-targeted therapeutics. In March 2013, we announced the acquisition of [18F]-HX4 [flortanidazole (18F)] from Siemens Healthcare. [18F]-HX4 is an investigational radiolabeled hypoxia Positron Emission Tomography (PET) tracer developed by Siemens Healthcare Molecular Imaging to potentially identify and quantify the degree of hypoxia in tumors *in vivo*. We initially intend to develop[18F]-HX4 to determine a patient's tumor hypoxia profile, which may identify patients who will best respond to our hypoxia-targeted therapeutics. We do not expect the acquisition of, or development activities related to, [18F]-HX4 to have a material impact on our results of operations in 2014.

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 since inception we have funded our operations through the private placement and public offering of equity securities and through payments received under our license and co-development agreement with Merck KGaA. As of December 31, 2013 and December 31, 2012, we had cash, cash equivalents and marketable securities of $82.0 million and $70.8 million, respectively.

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 under our collaboration with Merck KGaA or on

our own and continue our discovery efforts. Research and development expenses net of reimbursements of Merck KGaA's 70% share of total TH-302 development expenses are expected to increase in 2014 compared to 2013 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. Although 70% of the collaboration expenditures related to the development of TH-302 are expected to be funded by Merck KGaA, we expect that we will need to raise additional capital to complete the clinical development of TH-302 and to support new in-house development programs or to in-license or otherwise acquire and develop additional products or programs. 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 $12.5 million during the year ended December 31, 2013, from the amortization of the $110 million in upfront and milestone payments earned in 2012 and 2013 from our collaboration with Merck KGaA. 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.

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, 2013, 2012 and 2011

Revenue

For the year ended December 31, 2013, we recognized $12.5 million in revenue from the amortization of the aggregate of $110 million in upfront and milestone payments earned in 2013 and 2012 from our collaboration

with Merck KGaA. 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 payments earned in 2012 from our collaboration with Merck KGaA. 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 license agreement with Eleison for the development of glufosfamide, which represents our 50% share of an upfront payment from a sublicense by Eleison.

We expect revenue to increase in 2014 compared to 2013 due to the full year amortization of milestone payments earned in 2013.

Research and Development

Research and development expenses were $29.3 million for the year ended December 31, 2013, compared to $18.8 million for the year ended December 31, 2012 and $24.4 million for the year ended December 31, 2011. The $10.5 million increase in 2013 compared to 2012, net of reimbursement for Merck KGaA's 70% share of total development expenses for TH-302, was due primarily to a $6.4 million increase in TH-302 clinical development expenses, a $3.2 million increase in employee related expenses, including a $1.0 million increase in non-cash stock based compensation expense and a $0.9 million increase in consulting expenses. The $5.6 million decrease in 2012 compared to 2011 was due primarily to a $12.6 million reimbursement for Merck KGaA's 70% share of total development expenses for TH-302 and a $0.6 million decrease in consulting expenses, partially offset by a $4.1 million increase in clinical development expenses, a $2.4 million increase in employee-related expenses and a $1.1 million increase in non-cash stock based compensation.

During the years ended December 31, 2013, 2012 and 2011, we were engaged in two primary research and development programs: the development of TH-302, which is the subject of two ongoing pivotal Phase 3 clinical trials and multiple Phase 2 and Phase 1 clinical trials; and our discovery research program aimed at identifying new drug candidates. 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. The following table summarizes our research and development expenses (net of reimbursement for Merck KGaA's 70% share of total development expenses in the case of TH-302) attributable to both programs for each period presented:

	Years ended December 31,		
Research and development expenses by project (in thousands)	**2013**	**2012**	**2011**
TH-302	$ 24,675	$ 14,927	$ 20,692
Discovery research	4,659	3,859	3,696
Total research and development expenses	$ 29,334	$ 18,786	$ 24,388

Research and development expenses associated with TH-302 were $24.7 million net of the reimbursement for Merck KGaA's 70% share of total development expenses for TH-302 for 2013 compared to $14.9 million net of the reimbursement for Merck KGaA's 70% share of total development expenses for TH-302 for 2012, and $20.7 million for 2011. The increase of $9.8 million in 2013 compared to 2012, net of reimbursement for Merck KGaA's 70% share of total development expenses for TH-302, was due primarily to a $6.2 million increase in clinical development expenses, a $2.4 million increase in employee related expenses, including a $0.8 million increase in non-cash stock based compensation and a $1.2 million increase in consulting expenses. The decrease of $5.8 million in expenses in 2012 compared to 2011 was due primarily to a $12.6 million reimbursement for Merck KGaA's 70% share of total development expenses for TH-302 and a $0.5 million decrease in consulting expenses, partially offset by a $4.0 million increase in clinical development expenses, a $2.5 million increase in

employee-related expenses and a $0.8 million in non-cash stock based compensation. TH-302 continues to progress through the 406 trial, the MAESTRO trial conducted by Merck KGaA, the 404 trial, the 408 trial, the 410 trial and the 413 trial that was initiated during in August 2013.

Discovery research and development expenses were $4.7 million for 2013, $3.9 million for 2012 and $3.7 million for 2011. We continue to focus our efforts towards discovering and developing new drug candidates from our hypoxia activated prodrug platform.

The largest component of our total operating expenses is our ongoing investment in our research and development activities, including the clinical development of TH-302, and 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 KGaA's 70% share of development expenses, are expected to increase in 2014 compared to 2013 due to the continued execution of existing clinical trials and the start of new clinical trials. Expenses will fluctuate based upon many factors including the degree of collaborative activities, timing of manufacturing batches of TH-302 API and drug product, numbers of patients enrolled in our clinical trials and the outcome of each clinical trial event.

The process of conducting the clinical research necessary to obtain FDA and foreign regulatory approvals is costly, uncertain and time consuming. We consider the active management and development of our TH-302 and discovery research programs to be critical to our long-term success. The actual probability of success for TH-302 and future clinical product candidates may be impacted by a variety of factors, including, among others, the quality of the product candidate, early clinical data, investment in the program and the availability of adequate funding, competition, manufacturing capability and commercial viability. Furthermore, our strategy may include entering into collaborations with third parties, such as our TH-302 collaboration with Merck KGaA, to participate in the development and commercialization of our product candidates. In these situations, the preclinical development or clinical trial process for a product candidate and the estimated completion date may largely be under the control of that third party and not under our control. We cannot forecast with any degree of certainty which of our future clinical product candidates will be subject to future collaborations or how such arrangements would affect our development plans or capital requirements. In addition, the length of time required for clinical development of a particular product candidate and our development costs for that product candidate may be impacted by the scope and timing of enrollment in clinical trials for the product candidate, unanticipated additional clinical trials that may be required, future decisions to develop a product candidate for subsequent indications, and whether in the future we decide to pursue development of the product candidate with a collaborator or independently. For example, TH-302 may have the potential to be approved for multiple indications, and we do not yet know how many of those indications we and Merck KGaA will pursue. In this regard, the decision to pursue regulatory approval for subsequent indications will depend on several variables outside of our control, including the strength of the data generated in our and Merck KGaA's prior and ongoing clinical studies and the willingness of Merck KGaA to jointly fund such additional work. Furthermore, the scope and number of clinical studies required to obtain regulatory approval for each pursued indication is subject to the input of the applicable regulatory authorities, and we have not yet sought such input for all potential indications that we and Merck KGaA may elect to pursue, and even after having given such input applicable regulatory authorities may subsequently require additional clinical studies prior to granting regulatory approval based on new data generated by us or other companies, or for other reasons outside of our control.

The risks and uncertainties associated with our research and development projects are discussed more fully in Item 1A—Risk Factors. As a result of the risks and uncertainties discussed in Item 1A—Risk Factors and above, we are unable to determine with any degree of certainty the duration and completion costs of our research and development projects, anticipated completion dates or when and to what extent we will receive cash inflows from the commercialization and sale of a product candidate, including TH-302. To date, we have not commercialized any of our product candidates and in fact may never do so.

General and Administrative

General and administrative expenses were $9.2 million for 2013, compared to $7.1 million for 2012 and $5.7 million for 2011. The $2.1 million increase in 2013 compared to 2012 was primarily due to a $1.8 million increase in employee-related expenses, including a $0.9 million increase in non-cash stock-based compensation expense and a $0.3 million increase in consulting expenses. The $1.4 million increase in 2012 compared to 2011 reflects a $0.9 million increase in non-cash stock compensation expense, $0.7 million in higher consulting expenses and $0.3 million in higher staffing and facilities expenses, partially offset by a $0.5 million reimbursement of Merck KGaA'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 2014 compared to 2013 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 2013 was $0.1 million of interest income compared to $80,000 of net interest income for 2012 and $25,000 of net interest income for 2011. The increase in net interest income in both periods was primarily due to higher invested balances than the prior year.

Other Income (Expense)

Other income (expense) for 2013 was non-cash expense of $2.3 million compared to non-cash expense of $51.2 million for 2012 and non-cash income of $4.4 million for 2011. The decrease in non-cash expense in 2013 compared to 2012 was due to a smaller increase in the fair value of outstanding warrants to purchase common stock during 2013 compared to 2012, due to a smaller increase in the underlying stock price, and to a lesser extent, a decrease in the number of warrants outstanding during 2013 compared to 2012. 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 stock price. ASC 815 *"Derivatives and Hedging"* requires that stock warrants with certain terms need to 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 not generated and do not expect to generate revenue from sales of our product candidates in the near term. Since our inception, we have 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, 2013, we received approximately $1.9 million from the exercise of warrants to purchase approximately 2.4 million shares of common stock. During the year ended December 31, 2012, we sold an aggregate of approximately 2.0 million shares of common stock under our at market issuance sales agreement, or sales agreement, with MLV & Co., LLC, or MLV, 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.

To date we have received upfront and milestone payments of $110 million under our license and co-development agreement with Merck KGaA, including a $12.5 million in milestone payment received subsequent to December 31, 2013. We had cash, cash equivalents and marketable securities of $82.0 million and $70.8 million at December 31, 2013 and December 31, 2012, respectively, available to fund operations.

Net cash provided by operating activities for the years ended December 31, 2013 and 2012 was $10.2 million and $29.9 million, respectively, compared to net cash used in operating activities for the year ended

December 31, 2011 of $23.9 million. The $19.7 million decrease in net cash provided by operating activities in 2013 compared to 2012 was due to a $12.5 million decrease in milestone payments from the Merck KGaA collaboration in 2013 compared to 2012 and a $7.2 million increase in operating cash payments in 2013 compared to 2012. 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.

Net cash used in investing activities for the year ended December 31, 2013 was $16.3 million due primarily to purchases of marketable securities of $102.0 million, offset by proceeds from sales and maturities of investments of $85.8 million. 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 financing activities for the year ended December 31, 2013 was $2.4 million and was primarily due to the approximately $1.8 million proceeds from the exercise of warrants to purchase shares of common stock during 2013. 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.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our projected operating requirements for at least the next 12 months based upon current operating plans, milestone payment forecasts and spending assumptions. Although some of the expenditures related to TH-302 are expected to be funded by Merck KGaA, we expect that we will need to raise additional capital to complete the clinical development of TH-302 and to support new in-house development programs or 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, 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. In addition, our ability to raise additional capital may be dependent upon our common stock remaining listed on the NASDAQ Capital Market. 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.

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. We entered into a noncancelable facility sublease agreement for 28,650 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. In November 2013, we entered into a noncancelable facility lease agreement for 7,934 square feet of additional office space located in South San Francisco, California. The lease began on December 1, 2013 and will expire on December 31, 2016. The aggregate rent for the term of the lease is approximately $0.7 million.

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, 2013 are as follows (in thousands):

	One to three years (2014 to 2016)	Four to five years (2017 to 2018)	After five years	Total
Facilities leases	$ 2,699	$ 238	$ —	$2,937
Purchase commitments	2,628	—	—	2,628
Total	$ 5,327	$ 238	$ —	$5,565

At the Market Stock Issuance Facility

On October 29, 2010, we entered into an at market issuance sales agreement, or sales agreement, with 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. 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. In 2013, no shares were sold pursuant to the at market issuance sales agreement. As of December 31, 2013, shares of our common stock having an aggregate offering price of up to $2.7 million were still available for sale under the at market issuance sales agreement.

License and Development Agreements

On February 3, 2012, we entered into a global license and co-development agreement for TH-302 with Merck KGaA, Darmstadt, Germany, with an option to co-commercialize in the United States. Under the terms of the agreement, Merck KGaA received co-development rights, exclusive global commercialization rights and provided us with an option to co-commercialize TH-302 in the United States. To date we have received upfront and milestone payments of $110 million, including $12.5 million received subsequent to December 31, 2013. We can earn additional potential milestone payments of up to $440 million, comprised of $100 million in development and regulatory milestones and $340 million in sales-based milestones.

In the United States, we 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 in the United States 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 and product-by-product basis until the later of the last to expire patent covering such product containing 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 KGaA has the right to terminate the agreement upon limited notice, 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. Pursuant to the agreement we granted Eleison exclusive worldwide rights to manufacture, 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. We and Eleison 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 is responsible for all royalty and milestone payments due under certain agreements pursuant to which we licensed rights related to glufosfamide. The agreement contemplates that Eleison, to satisfy its diligence obligations, will raise sufficient funds to continue clinical development activities with glufosfamide.

Off-Balance Sheet Arrangements

As of December 31, 2013, 2012 and 2011, 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

For the year ended December 31, 2013, we recorded an income tax provision of $0.2 million, which was related to state minimum taxes. For the years ended December 31, 2012 and 2011, we did not record an income tax provision due to net operating losses and the inability to record an income tax benefit. As of December 31, 2013, we had accumulated approximately $81 million and $78 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 2015 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, 2013, we had research credit carryforwards of approximately $3.2 million and $4.3 million for federal and 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 2013 and 2012 revenues are related to our collaboration arrangement with Merck KGaA, which was entered in February 2012. Our collaboration with Merck KGaA 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 also receive reimbursement for Merck KGaA'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 our control. The deliverables under the Merck KGaA 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" in 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 with certain terms be classified as a liability and 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, which requires the use of significant judgment and estimates related to the inputs used in the model and can result in significant swings in the fair market valuation primarily due to changes in the price of our common stock. Since the outstanding common stock warrants are fair valued at the end of each reporting period, any significant 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 ten percent 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, 2013 and 2012, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2013. 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 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, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Threshold Pharmaceuticals, Inc., at December 31, 2013 and 2012, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, 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, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) and our report dated March 6, 2014, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Jose, California
March 6, 2014

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

	December 31, 2013	December 31, 2012
ASSETS		
Current assets:		
Cash and cash equivalents	$ 7,279	$ 11,029
Marketable securities, current	58,390	59,819
Collaboration receivable	18,094	15,635
Prepaid expenses and other current assets	2,246	1,167
Total current assets	86,009	87,650
Marketable securities, non-current	16,364	—
Property and equipment, net	686	812
Other assets	1,059	1,059
Total assets	$ 104,118	$ 89,521
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 1,689	$ 908
Accrued clinical and development expenses	7,444	5,750
Accrued liabilities	3,161	2,257
Deferred revenue, current	14,722	8,536
Total current liabilities	27,016	17,451
Warrant liability	23,421	32,558
Deferred revenue, non-current	76,916	53,097
Deferred rent	240	268
Total liabilities	127,593	103,374
Commitments and contingencies (Note 7)		
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value:		
Authorized: 2,000,000 shares; no shares issued and outstanding.	—	—
Common stock, $0.001 par value:		
Authorized: 150,000,000 shares at December 31, 2013 and 2012; Issued and outstanding: 59,232,611 and 56,431,207 shares at December 31, 2013 and 2012, respectively.	59	56
Additional paid-in capital	328,116	309,343
Accumulated other comprehensive (loss) income	28	11
Accumulated deficit	(351,678)	(323,263)
Total stockholders' equity (deficit)	(23,475)	(13,853)
Total liabilities and stockholders' equity (deficit)	$ 104,118	$ 89,521

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,		
	2013	2012	2011
Revenue	$ 12,495	$ 5,867	$ 62
Operating expenses:			
Research and development	29,334	18,786	24,388
General and administrative	9,185	7,080	5,710
Total operating expenses	38,519	25,866	30,098
Loss from operations	(26,024)	(19,999)	(30,036)
Interest income (expense), net	136	80	25
Other income (expense), net	(2,325)	(51,216)	4,358
Income (loss) before provision for income taxes	(28,213)	(71,135)	(25,653)
Provision for income taxes	202	—	—
Net loss	(28,415)	(71,135)	(25,653)
Other comprehensive income (loss):			
Unrealized gain (loss) on available for sale securities	17	12	(2)
Comprehensive loss	$ (28,398)	$ (71,123)	$ (25,655)
Net loss per common share:			
Basic	$ (0.49)	$ (1.31)	$ (0.56)
Diluted	$ (0.49)	$ (1.31)	$ (0.56)
Weighted average number of shares used in per common share calculations:			
Basic	57,832	54,219	45,900
Diluted	57,832	54,219	45,900

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, 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)
Exercise of warrants to purchase common stock	2,488,518	3	1,879	—	—	1,882
Issuance of common stock pursuant to stock plans	312,886	—	510	—	—	510
Stock-based compensation	—	—	4,922	—	—	4,922
Reclassification of fair value of warrants exercised from liability to equity	—	—	11,462	—	—	11,462
Change in unrealized gain (loss) on marketable securities	—	—	—	17	—	17
Net loss	—	—	—	—	(28,415)	(28,415)
Balances, December 31, 2013	59,232,611	59	328,116	28	(351,678)	(23,475)

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,		
	2013	2012	2011
Cash flows from operating activities:			
Net loss	$ (28,415)	$(71,135)	$(25,653)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,506	1,008	525
Stock-based compensation expense	4,922	3,010	1,039
Change in common stock warrant value	2,325	51,216	(4,358)
(Gain) loss on sale of investments, property and equipment	(5)	—	(17)
Changes in operating assets and liabilities:			
Collaboration receivable	(2,459)	(15,635)	—
Prepaid expenses and other current assets	(1,079)	(623)	(369)
Accounts payable	781	(1,481)	2,137
Accrued clinical and development expenses	1,694	1,285	2,026
Accrued liabilities	904	520	914
Deferred rent	(28)	115	(95)
Deferred revenue	30,005	61,633	—
Net cash provided by (used in) operating activities	10,151	29,913	(23,851)
Cash flows from investing activities:			
Acquisition of property and equipment	(158)	(482)	(528)
Acquisition of marketable securities	(101,968)	(93,745)	(28,154)
Proceeds from sales of marketable securities	5,338	14,266	2,037
Proceeds from maturities of marketable securities	80,495	33,285	17,463
Net cash provided by (used in) investing activities	(16,293)	(46,676)	(9,182)
Cash flows from financing activities:			
Proceeds from issuance of common stock and warrants, net of offering expenses	2,392	21,910	30,224
Net cash provided by provided by financing activities	2,392	21,910	30,224
Net increase (decrease) in cash and cash equivalents	(3,750)	5,147	(2,809)
Cash and cash equivalents, beginning of period	11,029	5,882	8,691
Cash and cash equivalents, end of period	$ 7,279	$ 11,029	$ 5,882
Non-cash investing and financing activities:			
Change in unrealized gain (loss) in marketable securities	$ 17	$ 12	$ (2)

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 using its expertise in the tumor microenvironment to discover and develop therapeutic agents that selectively target tumor cells for the treatment of patients living with cancer. 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, 2013, there has been no financial activity related to this entity.

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

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 are related to its collaboration arrangement with Merck KGaA, which was entered in February 2012. The collaboration with Merck KGaA 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 KGaA's 70% share for eligible worldwide development expenses for TH-302. Such reimbursement is reflected as a reduction of operating expenses.

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 KGaA 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. Significant estimates, assumptions and judgments made by management include those related to the valuation of equity and related instruments, revenue recognition, stock-based compensation and clinical trial accrued liabilities.

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.

The Company's investments are subject to a periodic impairment review. The Company recognizes an impairment charge when a decline in the fair value of its investments below the cost basis is judged to be other-than-temporary. The Company considers various factors in determining whether to recognize an impairment charge, including the length of time and extent to which the fair value has been less than the Company's cost basis, the financial condition and near-term prospects of the investee, and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value.

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 quoted market prices for the same or similar instruments. The counterparties to the agreements relating to the Company's investment securities consist of the US Treasury, various major corporations, governmental agencies and financial institutions with high credit standing.

Fair Value of Warrants

ASC 815 “Derivatives and Hedging” 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 common stock warrants with certain terms be classified as a liability and 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 outstanding common stock warrants using a Black Scholes valuation model at the end of each reporting period. The carrying amount of the common stock warrant liability represents its estimated fair value.

Concentration of Credit Risk

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.

Other Risks and Uncertainties

The Company has no products for commercial sale and has only one product candidate in clinical development 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. To date, the Company has received $110 million in upfront and milestone payments from this collaboration, including $12.5 million in milestone payments received subsequent to December 31, 2013. See further details in Note 3, “Collaboration Arrangements”.

The Company expects that it will need to raise additional capital to complete the clinical development of TH-302, to support 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;
- licensing arrangements; and/or
- public or private debt.

The Company’s ability to raise additional funds will depend, in part on the outcome of its 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 the Company’s control. In addition, the Company’s ability to raise additional capital may be dependent upon its common stock remaining listed on the NASDAQ Capital Market. The Company cannot be certain that sufficient funds will be available when required or on satisfactory terms, if at all. If adequate funds are not available, the Company may be required to significantly reduce or refocus its operations or to obtain funds through additional arrangements that may require the Company to relinquish rights to certain of our products, technologies or potential markets, any of which could delay or require that the Company curtail

or eliminate some or all of its development programs or otherwise have a material adverse effect on its business, financial condition and results of operations. In addition, the Company 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 its product candidates, if adequate funds are not available. 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.

The Company's lead product candidate, TH-302, has not received any regulatory approvals. To achieve profitable operations, the Company must successfully develop, test, manufacture and market its products, including TH-302. With respect to the development and commercialization of TH-302, the Company is substantially dependent on Merck KGaA for the continued development and potential commercialization of TH-302. There can be no assurance that TH-302 or any other product candidates 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.

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 or Merck KGaA is denied such approvals or such approvals are delayed, it could have a material adverse effect on the Company.

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. The Company reviews its property, plant and equipment assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

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 consist of costs such as salaries and benefits, laboratory supplies, facility costs, consulting fees and fees paid to contract research organizations, clinical trial sites, laboratories, other clinical service providers and contract manufacturing organizations. Research and development expenses are expensed as incurred.

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 results of operations 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.

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.

See Note 9 "Equity Incentive Plans and Stock Based Compensation" for further discussion.

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,		
	2013	2012	2011
Numerator:			
Net loss	$(28,415)	$(71,135)	$(25,653)
Denominator:			
Weighted-average number of common shares outstanding	57,832	54,219	45,900
Net loss per share:			
Basic	$ (0.49)	$ (1.31)	$ (0.56)
Diluted	$ (0.49)	$ (1.31)	$ (0.56)

The following warrants, outstanding options 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,		
	2013	2012	2011
Shares issuable upon exercise of warrants	8,282	11,583	16,643
Shares issuable upon exercise of stock options	6,527	5,099	3,672
Shares issuable related to the ESPP	64	79	70

NOTE 3—COLLABORATION ARRANGEMENTS

Agreement 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 KGaA received co-development rights, exclusive global commercialization rights and provided the Company with an option to co-commercialize TH-302 in the United States. To date the Company received $110 million in upfront and milestone payments, including $12.5 million received subsequent to December 31, 2013. 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 $100 million in regulatory and development milestones, and $340 million in commercialization milestones.

In the United States, the Company has 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 in the United States, 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 and product-by-product basis until the later of the last to expire patent covering such product containing 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 KGaA has the right to terminate the agreement on limited notice, 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 KGaA 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 KGaA 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 $42.5 million of milestones earned in 2013 and $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 $12.5 million and $5.9 million of revenue in 2013 and 2012, respectively. The Company will periodically review and, if necessary, revise the estimated periods of performance of our collaboration. The Company also earned a $16.5 million and $13.1 million reimbursement for eligible worldwide development expenses for TH-302 from Merck KGaA in 2013 and 2012, respectively. Such earned reimbursement has been reflected as a reduction of operating expenses.

Of the remaining potential future milestones, $100 million are related to regulatory and development milestones and $340 million are related to commercialization milestones that may be received under the Merck KGaA 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, that occurred subsequent to inception of the Merck KGaA agreement, 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 KGaA 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. If there are no future development obligations, the Company expects to 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 manufacture, 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 certain agreements pursuant to which the Company licensed rights related to glufosfamide. The agreement contemplates that Eleison, to satisfy its diligence obligations, will raise sufficient funds to continue clinical development activities with glufosfamide. There was no revenue in 2013 and 2012 from this agreement. In 2011, the Company received $0.1 million in revenue under the agreement, 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 available-for-sale marketable securities) at fair value on a recurring basis as of December 31, 2013 and 2012:

(in thousands)	Fair Value as of December 31, 2013	Basis of Fair Value Measurements		
		Level 1	Level 2	Level 3
Money market funds	$ 4,285	$ 4,285	$ —	$ —
Certificates of Deposit	1,584	—	1,584	
Corporate debt securities	49,019	—	49,019	—
Government securities	21,731	—	21,731	—
Municipal securities	2,815		2,815	
Commercial paper	2,599	—	2,599	—
Total cash equivalents and marketable securities	$ 82,033	$ 4,285	$ 77,748	$ —

(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	$ —

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, 2013 and 2012:

As of December 31, 2013 (in thousands):	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
Money market funds	$ 4,285	$ —	$ —	$ 4,285
Certificates of Deposit	1,584	—	—	1,584
Corporate debt securities	49,001	25	(7)	49,019
Government securities	21,722	12	(3)	21,731
Municipal securities	2,814	1	—	2,815
Commercial paper	2,599	—	—	2,599
	82,005	38	(10)	82,033
Less cash equivalents	7,279	—	—	7,279
Total marketable securities	$74,726	$ 38	$ (10)	$74,754

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

The Company recognized realized gains of $5,000 in 2013. There were no realized losses in 2013. There were no realized gains or losses in 2012 and 2011. The Company realized no gains in 2013 that were previously classified as unrealized gains and losses in accumulated other comprehensive income at December 31, 2012.

As of December 31, 2013, weighted average maturity for the Company's available for sale securities was approximately 6.4 months, with the longest maturity being May 2015.

The following table provides the breakdown of the marketable securities with unrealized losses at December 31, 2013 (in thousands):

As of December 31, 2013 (in thousands):	In loss position for less than twelve months	
	Fair Value	Unrealized Loss
Government securities	$ 2,898	$ (3)
Corporate debt securities	11,919	(7)
Total marketable securities	$14,817	$ (10)

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 8.3 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,	
	2013	2012
Computer and office equipment	$ 483	$ 436
Laboratory equipment	1,703	1,593
Leasehold improvements	523	523
	2,709	2,552
Less: Accumulated depreciation and amortization	(2,023)	(1,740)
Total property and equipment, net	$ 686	$ 812

Depreciation and amortization expense was $0.3 million, $0.2 million and $0.2 million for the years ended December 31, 2013, 2012 and 2011, respectively.

NOTE 6—BALANCE SHEET COMPONENTS

Accrued liabilities comprise the following (in thousands):

	December 31,	
	2013	2012
Payroll and employee related expenses	$ 2,682	$ 2,037
Professional services	150	122
Other accrued expenses	329	98
Total accrued liabilities	$ 3,161	$ 2,257

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.

The Company had a noncancelable facility sublease agreement for 28,650 square feet of laboratory space and office space located in South San Francisco, California, which serves as the Company's 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. In November 2013, the Company entered into a noncancelable facility lease agreement for 7,934 square feet of additional office space located in South San Francisco, California. The lease began on December 1, 2013 and will expire on December 31, 2016. The aggregate rent for the term of the lease is approximately $0.7 million.

As of December 31, 2013, the future rental payments required by the Company for these facilities under noncancelable operating leases are as follows (in thousands):

Years Ending December 31,	
2014	$ 828
2015	918
2016	953
2017	238
Thereafter	—
Total	$ 2,937

Rent expense for the years ended December 31, 2013, 2012 and 2011 was $0.6 million, $0.7 million and $1.3 million, respectively.

The Company's purchase commitments at December 31, 2013 were $2.6 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, 2013.

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 its 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 2011, the Company sold an aggregate of 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 its 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. In 2013, there were no shares sold pursuant to the at market issuance sales agreement. As of December 31, 2013, shares of the Company's common stock having an aggregate offering price of up to $2.7 million was still available for sale under the at market issuance sales agreement.

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 had 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 were subject to adjustment 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. As of August 29, 2013, all such warrants had been fully exercised.

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 2013, warrants to purchase 2,367,636 shares of common stock were cashless exercised for 1,555,043 shares of common stock. In addition, warrants to purchase 933,475 shares of common stock were exercised for net proceeds of approximately $1.9 million. In 2012, warrants to purchase 999,895 shares of common stock were cashless exercised for 666,793 shares of common stock. In addition, warrants to purchase 4,060,538 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 $11.5 million and $27.9 million from warrant liability into stockholders' equity in 2013 and 2012, respectively.

At December 31, 2013 and 2012, the Company had warrants outstanding to purchase 0 and 3,058,811 shares of common stock, respectively, from the August 2008 offering. The fair value of these warrants on December 31, 2013 and 2012 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2013	December 31, 2012
Risk-free interest rate	—	0.16%
Expected life (in years)	—	0.66
Dividend yield	—	—
Volatility	—	118%
Stock price	—	$ 4.21

During the years ended December 31, 2013, 2012 and 2011, a change in fair value of $2.4 million non-cash expense, $9.9 million non-cash income 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, 2013 and 2012, the Company had warrants outstanding to purchase 4,287,940 and 4,287,940 shares of common stock, respectively, from the October 2009 offering. The fair value of these warrants on December 31, 2013 and 2012 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2013	December 31, 2012
Risk-free interest rate	0.13%	0.25%
Expected life (in years)	0.76	1.76
Dividend yield	—	—
Volatility	49%	98%
Stock price	$ 4.67	$ 4.21

During the years ended December 31, 2013, 2012 and 2011, a change in fair value of $0.6 million of non-cash income, $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, 2013 and 2012 the Company had warrants outstanding to purchase 3,993,783 and 4,236,083 shares of common stock, respectively, from the March 2011 offering. The fair value of these warrants on December 31, 2013 and 2012 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2013	December 31, 2012
Risk-free interest rate	0.78%	0.72%
Expected life (in years)	2.21	3.21
Dividend yield	—	—
Volatility	88%	94%
Stock price	$ 4.67	$ 4.21

During the years ended December 31, 2013 and 2012, a change in the fair value of $0.5 million of non-cash expense, $17.1 million of non-cash income 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, 2013 and 2012:

	Fair Value as of December 31,	Basis of Fair Value Measurements		
(in thousands)	2013	Level 1	Level 2	Level 3
October 2009 warrants	$ 11,320	$ —	$ —	$ 11,320
March 2011 warrants	12,101	—	—	12,101
Total common stock warrants	$ 23,421	$ —	$ —	$ 23,421

	Fair Value as of December 31,	Basis of Fair Value Measurements		
(in thousands)	2012	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

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, 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
Exercise of common stock warrants during 2013	(11,462)
Change in fair value of common stock warrants during 2013	2,325
Balance at December 31, 2013	$ 23,421

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.

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, 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
Additional shares reserved	1,250,000	—		
Options granted	(1,663,500)	1,663,500	4.45–5.58	$ 5.10
Options exercised	—	(145,641)	0.79–3.46	$ 1.56
Options canceled	90,325	(90,325)	1.44–7.75	$ 6.49
Balances, December 31, 2013	175,236	6,526,506	$ 0.42–7.75	$ 3.66

At December 31, 2013, 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	570,518	4.22	$ 1.11	549,684	$ 1.10
$1.44 – 1.44	1,377,739	6.33	1.44	1,230,281	1.44
$1.49 – 1.64	1,124,003	7.36	1.63	715,809	1.63
$1.64 – 5.06	667,309	8.30	3.82	275,519	3.13
$5.09 – 5.09	1,185,000	9.19	5.09	236,249	5.09
$5.25 – 6.85	690,937	8.58	6.14	348,592	6.22
$7.00 – 7.75	911,000	8.32	7.26	366,536	7.25
$0.42 – 7.75	6,526,506	7.56	$ 3.66	3,722,760	$ 2.80

The aggregate intrinsic value of options outstanding and options exercisable as of December 31, 2013 were $10.5 million and $8.6 million, respectively. As of December 31, 2013, the ending options vested and expected to vest was 6,483,107 and the aggregate intrinsic value of these options was $10.5 million. The weighted average remaining contractual life and weighted average exercise price of these options were 7.55 years and $3.65, 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, 2013.

The total intrinsic value of stock options exercised during the years ended December 31, 2013, 2012 and 2011 were $0.5 million, $1.7 million and $6,000, respectively, determined at the date of the option exercise. Cash received from stock option exercises were $0.1 million, $0.6 million and $14,000 for the years ended December 31, 2013, 2012 and 2011, 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, 2013, employees had purchased 167,245 shares of common stock under the Purchase Plan at an average price of $1.69. 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. At December 31, 2013, plan participants had $0.3 million withheld to purchase stock on February 14, 2014, which is included in accrued liabilities on the accompanying consolidated balance sheet. At December 31, 2013, 235,896 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, which consists of the compensation cost for employee stock options and ESPP, and the value of options

issued to non-employees for services rendered, was allocated to research and development and general and administrative in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Stock-based compensation expense:			
Research and development	$ 2,562	$ 1,521	$ 471
General and administrative	2,360	1,489	568
	$ 4,922	$ 3,010	$ 1,039

Employee Stock-based Compensation Expense

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, 2013, 2012 and 2011:

	Years ended December 31,		
	2013	2012	2011
Employee Stock Options			
Risk-free interest rate	1.14%	1.12%	1.88%
Expected life (in years)	5.97	5.99	5.98
Dividend yield	—	—	—
Volatility	101%	105%	92%
Weighted-average fair value of stock options granted	$4.04	$5.09	$1.23
Employee Stock Purchase Plan			
Risk-free interest rate	0.19%	0.21%	0.15%
Expected life (in years)	1.25	1.25	1.25
Dividend yield	—	—	—
Volatility	77%	111%	80%
Weighted-average fair value of ESPP purchase rights	$2.27	$3.46	$0.66

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 considers its historical volatility 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.

The Company recognized $4.8 million, $2.8 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, 2013, 2012 and 2011, respectively. As of December 31, 2013, the total unrecognized compensation cost related to unvested stock-based awards granted to employees under the Company's stock option plans was approximately $10.3 million before estimated forfeitures. This cost will be recorded as compensation expense ratably over the remaining weighted average requisite service period of approximately 2.4 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,		
	2013	2012	2011
Risk-free interest rate	2.51%	1.93%	1.37%
Expected life (in years)	10	10	5.15
Dividend yield	—	—	—
Expected volatility	100%	101%	92%

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 $0.1 million, $0.2 million and $0.1 million for the years ended December 31, 2013, 2012 and 2011, respectively.

NOTE 10—INCOME TAXES

For the year ended December 31, 2013, the Company recorded an income tax provision of $0.2 million, which was related to state minimum taxes. For the years ended December 31, 2012 and 2011, the Company did not record an income tax provision due to net operating losses and the inability to record an income tax benefit.

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):

	2013	2012	2011
U.S. federal taxes (benefit) at statutory rate	$(9,592)	$(24,186)	$ (8,722)
State federal income tax benefit	(1,794)	(1,160)	(1,995)
Unutilized (utilized) net operating losses	9,747	7,455	11,731
Stock-based compensation	486	288	223
Research and development credits	(1,416)	—	(885)
Tax assets not benefited	1,926	143	1,105
Nondeductible warrant expense	790	17,414	(1,482)
Other	55	46	25
Total	$ 202	$ —	$ —

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,	
	2013	2012
Capitalized start-up costs	$ 179	$ 209
Net operating loss carryforwards	31,988	44,769
Research and development credits	5,427	3,513
Deferred stock compensation	3,327	2,115
Deferred revenue	21,151	—
Other (accruals, reserves, depreciation)	1,069	958
Total deferred tax assets	63,141	51,564
Less: Valuation allowance	(63,141)	(51,564)
	$ —	$ —

At December 31, 2013, the Company had federal and state net operating loss carryforwards of approximately $81 million and $78 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 2015, 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 balance as of December 31, 2013 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, 2013, the Company had federal research and development tax credits of approximately $3.2 million, which expire in the year beginning 2022, and state research and development tax credits of approximately $4.3 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 $11.6 million, $7.8 million and by $11.6 million for the years ended December 31, 2013, 2012 and 2011, 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)	2013	2012
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, 2013 and 2012, 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, 2013, 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, 2013. 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.

2013	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share data)				
Revenue	$ 2,922	$ 3,180	$3,181	$ 3,212
Net income (loss)	$ (9,214)	$(12,788)	$1,176	$ (7,589)
Net income (loss) per common share				
Basic	$ (0.16)	$ (0.22)	$ 0.02	$ (0.13)
Diluted	$ (0.16)	$ (0.22)	$ (0.08)	$ (0.13)

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)

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, 2013, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, 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 principal executive officer and principal financial officer is appropriate, to allow timely decisions, regarding required disclosure. Based upon that evaluation, our principal executive officer and principal financial officer 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 principal executive officer and our principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on criteria established in the *Internal Control—Integrated Framework* (1992 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, 2013.

Our independent registered public accounting firm, Ernst & Young LLP, has audited our internal control over financial reporting as of December 31, 2013. 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 principal executive officer and principal financial officer, 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 our company 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, 2013 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, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) (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, 2013, 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, 2013 and 2012, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2013 of Threshold Pharmaceuticals, Inc. and our report dated March 6, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Jose, California
March 6, 2014

ITEM 9B. OTHER INFORMATION

None.

PART III

The information required by Part III is omitted from this report because we will file a definitive proxy statement within 120 days after the end of our 2013 fiscal year pursuant to Regulation 14A for our 2014 Annual Meeting of Stockholders, or the 2014 Proxy Statement, and the information to be included in the 2014 Proxy Statement is incorporated herein by reference.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be contained in the 2014 Proxy Statement and is hereby incorporated by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be contained in the 2014 Proxy Statement 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 the 2014 Proxy Statement 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 the 2014 Proxy Statement and is hereby incorporated by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item will be contained in the 2014 Proxy Statement 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 report of Ernst & Young 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.

(3) A list of exhibits filed with this report or incorporated herein by reference is found in the Exhibit Index immediately following the signature page of this Annual Report.

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 6, 2014

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

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Harold E. Selick, Ph.D. and Joel A. Fernandes, and each of them, with full power to act without the other, such person's true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Form 10-K, and to file the same, with exhibits and schedules thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing necessary or desirable to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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 6, 2014
/s/ JOEL A. FERNANDES **Joel A. Fernandes**	Vice President, Finance and Controller (principal financial and accounting officer)	March 6, 2014
/s/ JEFFREY W. BIRD, M.D., PH.D. **Jeffrey W. Bird, M.D., Ph.D.**	Director	March 6, 2014
/s/ BRUCE C. COZADD **Bruce C. Cozadd**	Director	March 6, 2014
/s/ DAVID R. HOFFMANN **David R. Hoffmann**	Director	March 6, 2014
/s/ WILFRED E. JAEGER, M.D. **Wilfred E. Jaeger, M.D.**	Director	March 6, 2014
/s/ GEORGE G. C. PARKER, PH.D. **George G. C. Parker, Ph.D.**	Director	March 6, 2014
/s/ DAVID R. PARKINSON, M.D. **David R. Parkinson, M.D.**	Director	March 6, 2014

EXHIBIT INDEX

EXHIBIT NUMBER	DESCRIPTION
3.1*	Amended and Restated Certificate of Incorporation of the Registrant, as subsequently amended
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-114376), filed on April 9, 2004)
4.1	Specimen Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to Amendment No. 6 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-114376), filed on January 28, 2005)
4.2	Preferred Shares Rights Agreement, dated as of August 8, 2006, by and between Registrant and Mellon Investor Services LLC (incorporated by reference to Exhibit 4.5 to the Registrant's Current Report on Form 8-K filed on August 9, 2006)
4.3	Form of Rights Certificate (incorporated by reference to Exhibit 4.6 to the Registrant's Current Report on Form 8-K filed on August 9, 2006)
4.4	Amendment to Rights Agreement, dated as of July 10, 2008, between the Registrant and Mellon Investor Services LLC (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed on July 14, 2008)
4.5	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 the Registrant's Current Report on Form 8-K filed on September 30, 2009)
4.6	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 the Registrant's Current Report on Form 8-K filed on March 11, 2011)
4.7	Form of Warrant issued pursuant to the Securities Purchase Agreement, dated as of September 29, 2009, by and among the Registrant and the investors named therein (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on September 30, 2009)
4.8	Form of Warrant issued pursuant to the Registrant's prospectus supplement, dated March 11, 2011, and accompanying prospectus (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on March 11, 2011)
10.1+	2004 Amended and Restated Equity Incentive Plan of the Registrant, as amended (incorporated by reference to Exhibit 10.2 to the Registrant's Annual Report on Form 10-K filed on March 15, 2012)
10.2+	2004 Employee Stock Purchase Plan of the Registrant As Amended and Restated Effective May 22, 2009 (incorporated by reference to Exhibit 99.2 to the Registrant's Registration Statement on Form S-8 (File No. 333-164865) filed on February 11, 2010)
10.3+	Form of Indemnification Agreement by and between the Registrant and its officers and directors (incorporated by reference to Exhibit 10.9 to Amendment No. 3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-114376), filed on December 6, 2004)
10.4+	Form of Notice of Grant of Stock Options and Option Agreement (incorporated by reference to Exhibit 10.25 to the Registrant's Current Report on Form 8-K filed on March 17, 2006)
10.5+	Offer Letter by and between the Registrant and Joel A. Fernandes dated November 1, 2007 (incorporated by reference to Exhibit 10.36 to the Registrant's Current Report on Form 8-K filed on November 2, 2007)

EXHIBIT NUMBER	DESCRIPTION
10.6	Form of Securities Purchase Agreement, dated July 9, 2008, by and among the Registrant and the investors party thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on July 14, 2008)
10.7+	Form of Amended and Restated Change of Control Severance Agreement (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on April 12, 2012)
10.8+	Change of Control Severance Agreement by and between the Registrant and Tillman E. Pearce, dated as of April 9, 2012, (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on April 12, 2012)
10.9†	Exclusive License Agreement, effective as of October 5, 2009, by and between the Registrant and Eleison Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.26 to the Registrant's Annual Report on Form 10-K filed on March 8, 2010)
10.10†	License and Co-Development Agreement between the Registrant and Merck KGaA, dated February 2, 2012 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed on August 6, 2012)
10.11*††	Amendment to License and Co-Development Agreement between the Registrant and Merck KGaA, dated December 2, 2013.
10.12	At Market Issuance Sales Agreement by and between the Registrant and McNicoll, Lewis & Vlak LLC (predecessor to MLV & Co., LLC), dated October 29, 2010 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on October 29, 2010)
10.13	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 the Registrant's Current Report on Form 8-K filed on January 20, 2012)
10.14	Sublease by and between the Registrant and Exelixis, Inc. dated as of July 25, 2011 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed on November 3, 2011)
23.1*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities and Exchange Act of 1934, as amended, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities and Exchange Act of 1934, as amended, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2**	Certification of Principal Financial Officer 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
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document

EXHIBIT NUMBER	DESCRIPTION
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.

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

+ Indicates a management contract or compensatory plan or arrangement.

** Furnished herewith. This certification is not deemed filed for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, and is not deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act.

Exhibit 3.1

AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
THRESHOLD PHARMACEUTICALS, INC.

Threshold Pharmaceuticals, Inc., a corporation, organized and existing under the laws of the State of Delaware (the "***Corporation***"), hereby certifies as follows:

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

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

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

4. A Certificate of Amendment of the Amended and Restated Certificate of Incorporation was filed with the Secretary of State of Delaware on January 26, 2005.

5. The Amended and Restated Certificate of Incorporation in the form attached hereto as Exhibit A has been duly adopted in accordance with the provisions of Sections 242, 245 and 228 of the General Corporation Law of the State of Delaware by the directors and stockholders of the Corporation, and prompt written notice was duly given pursuant to Section 228 to those stockholders who did not approve the Amended and Restated Certificate of Incorporation by written consent.

6. The Amended and Restated Certificate of Incorporation so adopted reads in full as set forth in Exhibit A attached hereto and is hereby incorporated herein by this reference.

IN WITNESS WHEREOF, Threshold Pharmaceuticals, Inc. has caused this Certificate to be signed by the Chief Financial Officer this 9th day of February, 2005.

THRESHOLD PHARMACEUTICALS, INC.

By: /s/ Janet I. Swearson
Janet I. Swearson, Chief Financial Officer

EXHIBIT A

AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
THRESHOLD PHARMACEUTICALS, INC.

FIRST

The name of the Corporation is Threshold Pharmaceuticals, Inc.

SECOND

The address of the registered office of the Corporation in the State of Delaware is Corporation Trust Center, 1209 Orange Street, Wilmington, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

THIRD

The purpose of the Corporation is to engage in any lawful act or activity for which a corporation may be organized under the Delaware General Corporation Law.

FOURTH

A. The total number of shares of all classes of stock which the Corporation shall have authority to issue is 152,000,000, consisting of 150,000,000 shares of Common Stock, par value $0.001 per share (the "Common Stock") and 2,000,000 shares of Preferred Stock, par value $0.001 per share (the "Preferred Stock").

B. The board of directors is authorized, subject to any limitations prescribed by law, to provide for the issuance of shares of Preferred Stock in one or more series, and by filing a certificate pursuant to the applicable law of the State of Delaware (such certificate being hereinafter referred to as a "Preferred Stock Designation"), to establish from time to time the number of shares to be included in each such series, and to fix the designation, powers, preferences, and rights of the shares of each such series and any qualifications, limitations or restrictions thereof. The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the Common Stock, without a vote of the holders of the Preferred Stock, or of any series thereof, unless a vote of any such holders is required pursuant to the terms of any Preferred Stock Designation.

C. Each outstanding share of Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the Corporation for their vote; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (including any

Certificate of Designations relating to any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon by law or pursuant to this Certificate of Incorporation (including any Certificate of Designations relating to any series of Preferred Stock).

FIFTH

The following provisions are inserted for the management of the business and the conduct of the affairs of the Corporation, and for further definition, limitation and regulation of the powers of the Corporation and of its directors and stockholders:

A. The business and affairs of the Corporation shall be managed by or under the direction of the board of directors. In addition to the powers and authority expressly conferred upon them by statute or by this Certificate of Incorporation or the bylaws of the Corporation, the directors are hereby empowered to exercise all such powers and do all such acts and things as may be exercised or done by the Corporation.

B. The directors of the Corporation need not be elected by written ballot unless the bylaws so provide.

C. Any action required or permitted to be taken by the stockholders of the Corporation must be effected at a duly called annual or special meeting of stockholders of the Corporation and may not be effected by any consent in writing by such stockholders.

D. Special meetings of stockholders of the Corporation may be called only by the Chairman of the Board or the President or by the board of directors acting pursuant to a resolution adopted by a majority of the Whole Board. For purposes of this Certificate of Incorporation, the term "Whole Board" shall mean the total number of authorized directors whether or not there exist any vacancies in previously authorized directorships.

E. In addition to the requirements of law and any other provisions hereof (and notwithstanding the fact that approval by a lesser vote may be permitted by law or any other provision thereof), the affirmative vote of the holders of at least 66 2/3% of the voting power of the then-outstanding stock shall be required to amend, alter, repeal or adopt any provision inconsistent with this Sections C, D and E of this Article Fifth.

SIXTH

A. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the number of directors shall be fixed from time to time exclusively by the board of directors pursuant to a resolution adopted by a majority of the Whole Board. The directors, other than those who may be elected by the holders of any series of Preferred Stock under specified circumstances, shall be divided into three classes, with the term of office of the first class to expire at the Corporation's first annual meeting of stockholders following the first sale of the Corporation's Common Stock pursuant to a firmly underwritten registered public offering (the "IPO"), the term of office of the second class to expire at the Corporation's second annual meeting of stockholders following the IPO and the

term of office of the third class to expire at the Corporation's third annual meeting of stockholders following the IPO, and thereafter for each such term to expire at each third succeeding annual meeting of stockholders after such election and with each director to hold office until his or her successor shall have been duly elected and qualified. At each annual meeting of stockholders, directors elected to succeed those directors whose terms expire shall be elected for a term of office to expire at the third succeeding annual meeting of stockholders after their election, with each director to hold office until his or her successor shall have been duly elected and qualified.

B. Subject to the rights of the holders of any series of Preferred Stock then outstanding, newly created directorships resulting from any increase in the authorized number of directors or any vacancies in the board of directors resulting from death, resignation, retirement, disqualification, removal from office or other cause shall, unless otherwise required by law or by resolution of the board of directors, be filled only by a majority vote of the directors then in office, though less than a quorum (and not by stockholders), and directors so chosen shall serve for a term expiring at the annual meeting of stockholders at which the term of office of the class to which they have been chosen expires or until such director's successor shall have been duly elected and qualified. No decrease in the authorized number of directors shall shorten the term of any incumbent director.

C. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the Corporation shall be given in the manner provided in the bylaws of the Corporation.

D. In addition to the requirements of law and any other provisions hereof (and notwithstanding the fact that approval by a lesser vote may be permitted by law or any other provision thereof), the affirmative vote of the holders of at least 66 2/3% of the voting power of the then-outstanding stock shall be required to amend, alter, repeal or adopt any provision inconsistent with this Article Sixth.

SEVENTH

The board of directors is expressly empowered to adopt, amend or repeal the bylaws of the Corporation. Any adoption, amendment or repeal of the bylaws of the Corporation by the board of directors shall require the approval of a majority of the Whole Board. The stockholders shall also have power to adopt, amend or repeal the bylaws of the Corporation; provided, however, that, in addition to any vote of the holders of any class or series of stock of the Corporation required by law or by this Certificate of Incorporation, the affirmative vote of the holders of at least 66 2/3% of the voting power of all of the then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required for the stockholders to adopt, amend or repeal any provision of the bylaws of the Corporation. In addition to the requirements of law and any other provisions hereof (and notwithstanding the fact that approval by a lesser vote may be permitted by law or any other provision thereof), the affirmative vote of the holders of at least 66 2/3% of the voting power of the then-outstanding stock shall be required to amend, alter, repeal or adopt any provision inconsistent with this Article Seventh.

EIGHTH

A director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the Corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the Delaware General Corporation Law, or (iv) for any transaction from which the director derived an improper personal benefit. If the Delaware General Corporation Law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

Any repeal or modification of the foregoing paragraph by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of such repeal or modification.

NINTH

The Corporation reserves the right to amend or repeal any provision contained in this Certificate of Incorporation in the manner now or hereafter prescribed by the laws of the State of Delaware and all rights conferred upon stockholders are granted subject to this reservation.

CERTIFICATE OF DESIGNATIONS

OF RIGHTS, POWERS AND PREFERENCES OF

SERIES A PARTICIPATING PREFERRED STOCK

OF

THRESHOLD PHARMACEUTICALS, INC.

Pursuant to Section 151(g) and Section 103 of the General Corporation Law of the State of Delaware, I, Harold E. Selick, the Chief Executive Officer, of Threshold Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under the General Corporation Law of the State of Delaware hereby certify:

That pursuant to the authority conferred upon the Board of Directors by the Amended and Restated Certificate of Incorporation of the Corporation, the Board of Directors, on August 8, 2006 adopted the following resolution creating a series of shares of Preferred Stock designated as Series A Participating Preferred Stock:

"RESOLVED: that pursuant to the authority vested in the Board of Directors of the Corporation by the Amended and Restated Certificate of Incorporation (the "Restated Certificate"), the Board of Directors does hereby provide for the issue of a series of Preferred Shares, $0.001 par value, of the Corporation, to be designated "Series A Participating Preferred Stock", initially consisting of Two Hundred Thousand (200,000) shares and to the extent that the designations, powers, preferences and relative and other special rights and the qualifications, limitations and restrictions of the Series A Participating Preferred Stock are not stated and expressed in the Restated Certificate, does hereby fix and herein state and express such designations, powers, preferences and relative and other special rights and the qualifications, limitations and restrictions thereof, as follows (all terms used herein which are defined in the Restated Certificate shall be deemed to have the meanings provided therein):

1. **Designation and Amount.** The shares of such series shall be designated as "Series A Participating Preferred Stock", par value $0.001 per share, and the number of shares constituting such series shall be Two Hundred Thousand (200,000). Such number of shares may be increased or decreased by resolution of the Board of Directors; provided, however, that no decrease shall reduce the number of shares of Series A Participating Preferred Stock to a number of shares less than the number of shares then outstanding plus the number of shares reserved for issuance upon the exercise of outstanding options, rights or warrants or upon the conversion of any outstanding securities issued by the Corporation convertible into Series A Participating Preferred Stock.

2. **Dividends and Distributions.**

(A) Subject to the prior and superior right of the holders of any shares of any series of Preferred Stock ranking prior and superior to the shares of Series A Participating Preferred Stock with respect to dividends, the holders of shares of Series A Participating Preferred Stock shall be entitled to receive when, as and if declared by the Board of Directors out

of funds legally available for the purpose, quarterly dividends payable in cash on the last day of March, June, September and December in each year (each such date being referred to herein as a "Quarterly Dividend Payment Date"), commencing on the first Quarterly Dividend Payment Date after the first issuance of a share or fraction of a share of Series A Participating Preferred Stock, in an amount per share (rounded to the nearest cent) equal to, subject to the provision for adjustment hereinafter set forth, 1,000 times the aggregate per share amount of all cash dividends, and 1,000 times the aggregate per share amount (payable in kind) of all non-cash dividends or other distributions other than a dividend payable in shares of Common Stock or a subdivision of the outstanding shares of Common Stock (by reclassification or otherwise), declared on the Common Stock of the Corporation (the "Common Stock") since the immediately preceding Quarterly Dividend Payment Date, or, with respect to the first Quarterly Dividend Payment Date, since the first issuance of any share or fraction of a share of Series A Participating Preferred Stock. In the event the Corporation shall at any time after August 8, 2006 (the "Rights Declaration Date") (i) declare any dividend on Common Stock payable in shares of Common Stock, (ii) subdivide the outstanding Common Stock, or (iii) combine or consolidate the outstanding Common Stock into a smaller number of shares, then in each such case the amount to which holders of shares of Series A Participating Preferred Stock were entitled immediately prior to such event under the preceding sentence shall be adjusted by multiplying such amount by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) The Corporation shall declare a dividend or distribution on the Series A Participating Preferred Stock as provided in paragraph (A) above immediately after it declares a dividend or distribution on the Common Stock (other than a dividend payable in shares of Common Stock).

(C) Dividends shall begin to accrue and be cumulative on outstanding shares of Series A Participating Preferred Stock from the Quarterly Dividend Payment Date next preceding the date of issue of such shares of Series A Participating Preferred Stock, unless the date of issue of such shares is prior to the record date for the first Quarterly Dividend Payment Date, in which case dividends on such shares shall begin to accrue from the date of issue of such shares, or unless the date of issue is a Quarterly Dividend Payment Date or is a date after the record date for the determination of holders of shares of Series A Participating Preferred Stock entitled to receive a quarterly dividend and before such Quarterly Dividend Payment Date, in either of which events such dividends shall begin to accrue and be cumulative from such Quarterly Dividend Payment Date. Accrued but unpaid dividends shall not bear interest. Dividends paid on the shares of Series A Participating Preferred Stock in an amount less than the total amount of such dividends at the time accrued and payable on such shares shall be allocated pro rata on a share-by-share basis among all such shares at the time outstanding. The Board of Directors may fix a record date for the determination of holders of shares of Series A Participating Preferred Stock entitled to receive payment of a dividend or distribution declared thereon, which record date shall be no more than 60 days prior to the date fixed for the payment thereof.

3. **Voting Rights.** The holders of shares of Series A Participating Preferred Stock shall have the following voting rights:

(A) Subject to the provision for adjustment hereinafter set forth, each share of Series A Participating Preferred Stock shall entitle the holder thereof to 1,000 votes on all matters submitted to a vote of the stockholders of the Corporation. In the event the Corporation shall at any time after the Rights Declaration Date (i) declare or pay any dividend on Common Stock payable in shares of Common Stock, (ii) subdivide the outstanding Common Stock, or (iii) combine the outstanding Common Stock into a smaller number of shares, then in each such case the number of votes per share to which holders of shares of Series A Participating Preferred Stock were entitled immediately prior to such event shall be adjusted by multiplying such number by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) Except as otherwise provided herein, in the Restated Certificate, or by law, the holders of shares of Series A Participating Preferred Stock and the holders of shares of Common Stock, and any other capital stock of the Corporation having general voting rights, shall vote together as one class on all matters submitted to a vote of stockholders of the Corporation.

(C) Except as required by law, holders of Series A Participating Preferred Stock shall have no special voting rights and their consent shall not be required (except to the extent they are entitled to vote with holders of Common Stock as set forth herein) for taking any corporate action.

4. **Certain Restrictions.**

(A) The Corporation shall not declare any dividend on, make any distribution on, or redeem or purchase or otherwise acquire for consideration any shares of Common Stock after the first issuance of a share or fraction of a share of Series A Participating Preferred Stock unless concurrently therewith it shall declare a dividend on the Series A Participating Preferred Stock as required by Section 2 hereof.

(B) Whenever quarterly dividends or other dividends or distributions payable on the Series A Participating Preferred Stock as provided in Section 2 are in arrears, thereafter and until all accrued and unpaid dividends and distributions, whether or not declared, on shares of Series A Participating Preferred Stock outstanding shall have been paid in full, the Corporation shall not:

(i) declare or pay dividends on, make any other distributions on, or redeem or purchase or otherwise acquire for consideration any shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Series A Participating Preferred Stock;

(ii) declare or pay dividends on, make any other distributions on any shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with Series A Participating Preferred Stock, except dividends paid ratably on the Series A Participating Preferred Stock and all such parity stock on which dividends are payable or in arrears in proportion to the total amounts to which the holders of all such shares are then entitled;

(iii) redeem or purchase or otherwise acquire for consideration shares of any stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Series A Participating Preferred Stock, provided that the Corporation may at any time redeem, purchase or otherwise acquire shares of any such parity stock in exchange for shares of any stock of the Corporation ranking junior (either as to dividends or upon dissolution, liquidation or winding up) to the Series A Participating Preferred Stock;

(iv) purchase or otherwise acquire for consideration any shares of Series A Participating Preferred Stock, or any shares of stock ranking on a parity with the Series A Participating Preferred Stock, except in accordance with a purchase offer made in writing or by publication (as determined by the Board of Directors) to all holders of such shares upon such terms as the Board of Directors, after consideration of the respective annual dividend rates and other relative rights and preferences of the respective series and classes, shall determine in good faith will result in fair and equitable treatment among the respective series or classes.

(C) The Corporation shall not permit any subsidiary of the Corporation to purchase or otherwise acquire for consideration any shares of stock of the Corporation unless the Corporation could, under paragraph (A) of this Section 4, purchase or otherwise acquire such shares at such time and in such manner.

5. **Reacquired Shares.** Any shares of Series A Participating Preferred Stock purchased or otherwise acquired by the Corporation in any manner whatsoever shall be retired and canceled promptly after the acquisition thereof. All such shares shall upon their cancellation become authorized but unissued shares of Preferred Stock and may be reissued as part of a new series of Preferred Stock to be created by resolution or resolutions of the Board of Directors, subject to the conditions and restrictions on issuance set forth herein or in the Restated Certificate, or as otherwise required by law.

6. **Liquidation, Dissolution or Winding Up.**

(A) Upon any liquidation (voluntary or otherwise), dissolution or winding up of the Corporation, no distribution shall be made to the holders of shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Series A Participating Preferred Stock unless, prior thereto, the holders of shares of Series A Participating Preferred Stock shall have received an amount equal to accrued and unpaid dividends and distributions thereon, whether or not declared, to the date of such payment, plus an amount equal to the greater of (1) $1,000 per share, provided that in the event the Corporation does not have sufficient assets, after payment of its liabilities and distribution to holders of Preferred Stock ranking prior to the Series A Participating Preferred Stock, available to permit payment in full of the $1,000 per share amount, the amount required to be paid under this Section 6(A)(1) shall, subject to Section 6(B) hereof, equal the value of the amount of available assets divided by the number of outstanding shares of Series A Participating Preferred Stock or (2) subject to the provisions for adjustment hereinafter set forth, 1,000 times the aggregate per share amount to be distributed to the holders of Common Stock (the greater of (1) or (2), the "Series A Liquidation Preference"). In the event the Corporation shall at any time after the Rights Declaration Date (i) declare any dividend on Common Stock payable in shares of Common Stock, (ii) subdivide the outstanding Common Stock, or (iii) combine or consolidate the outstanding Common Stock into

a smaller number of shares, then in each such case the amount to which holders of shares of Series A Participating Preferred Stock were entitled immediately prior to such event under clause (2) of the preceding sentence shall be adjusted by multiplying such amount by a fraction the numerator of which is the number of shares of Common Stock that were outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) In the event, however, that there are not sufficient assets available to permit payment in full of the Series A Liquidation Preference and the liquidation preferences of all other series of Preferred Stock, if any, which rank on a parity with the Series A Participating Preferred Stock, then such remaining assets shall be distributed ratably to the holders of such parity shares in proportion to their respective liquidation preferences.

7. **Consolidation, Merger, etc.** In case the Corporation shall enter into any consolidation, merger, combination or other transaction in which the shares of Common Stock are exchanged for or changed into other stock or securities, cash and/or any other property, then in any such case the shares of Series A Participating Preferred Stock shall at the same time be similarly exchanged or changed in an amount per share (subject to the provision for adjustment hereinafter set forth) equal to 1,000 times the aggregate amount of stock, securities, cash and/or any other property (payable in kind), as the case may be, into which or for which each share of Common Stock is changed or exchanged. In the event the Corporation shall at any time after the Rights Declaration Date (i) declare any dividend on Common Stock payable in shares of Common Stock, (ii) subdivide the outstanding Common Stock, or (iii) combine or consolidate the outstanding Common Stock into a smaller number of shares, then in each such case the amount set forth in the preceding sentence with respect to the exchange or change of shares of Series A Participating Preferred Stock shall be adjusted by multiplying such amount by a fraction the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of common Stock that were outstanding immediately prior to such event.

8. **No Redemption.** The shares of Series A Participating Preferred Stock shall not be redeemable.

9. **Ranking.** The Series A Participating Preferred Stock shall rank junior to all other series of the Corporation's Preferred Stock as to the payment of dividends and the distribution of assets, unless the terms of any such series shall provide otherwise.

10. **Amendment.** The Certificate of Incorporation of the Corporation shall not be further amended in any manner, including by merger or consolidation, which would materially alter or change the powers, preference or special rights of the Series A Participating Preferred Stock so as to affect them adversely without the affirmative vote of the holders of a majority or more of the outstanding shares of Series A Participating Preferred Stock, voting together as a single class.

11. **Fractional Shares.** Series A Participating Preferred Stock may be issued in fractions of a share which shall entitle the holder, in proportion to such holder's fractional shares, to exercise voting rights, receive dividends, participate in distributions and to have the benefit of all other rights of holders of Series A Participating Preferred Stock."

Executed this 9th day of August, 2006.

/s/ Harold E. Selick
Harold E. Selick
Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF THE
AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
THRESHOLD PHARMACEUTICALS, INC.

The undersigned, Dr. Harold E. Selick, hereby certifies that:

1. He is the Chief Executive Officer of Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Corporation").

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

3. Article Fourth, Paragraph A of the Corporation's Amended and Restated Certificate of Incorporation is amended and restated in its entirety to read as follows:

> "A. The total number of shares of all classes of stock which the Corporation shall have authority to issue is 52,000,000, consisting of 50,000,000 shares of Common Stock, par value $0.001 per share (the "Common Stock") and 2,000,000 shares of Preferred Stock, par value $0.001 per share (the "Preferred Stock").
>
> On August 20, 2008, at 12:01 a.m. EST (the "Effective Time"), each six shares of the Corporation's Common Stock issued and outstanding immediately prior to the Effective Time shall be reclassified and combined into one share of the Corporation's Common Stock, automatically and without any action on the part of the respective holders thereof (the "Reverse Stock Split"). No fractional shares shall be issued in the Reverse Stock Split. In lieu of issuing fractional shares, the aggregate of all fractional shares otherwise issuable in the Reverse Stock Split shall be issued to the Corporation's transfer agent, as agent for the accounts of all holders of such fractional shares. The transfer agent shall sell all of the fractional interests as soon as practicable after the Effective Time on the basis of the prevailing market prices on the open market on behalf of such holders, and then pay each such holder his, her or its pro rata portion of the sale proceeds."

4. This Certificate of Amendment of the Corporation's Amended and Restated Certificate of Incorporation has been duly adopted by this Corporation's Board of Directors and stockholders in accordance with the provisions of the Corporation's Amended and Restated Certificate of Incorporation and with Section 242 of the General Corporation Law of the State of Delaware.

IN WITNESS WHEREOF, the undersigned has executed this Certificate of Amendment of Amended and Restated Certificate of Incorporation at Redwood City, California on August 18, 2008.

/s/ Dr. Harold E. Selick
Dr. Harold E. Selick
Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF THE
AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
THRESHOLD PHARMACEUTICALS, INC.

The undersigned, Dr. Harold E. Selick, hereby certifies that:

1. He is the Chief Executive Officer of Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Corporation").

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

3. Article Fourth, Paragraph A of the Corporation's Amended and Restated Certificate of Incorporation is amended and restated in its entirety to read as follows:

> "A. The total number of shares of all classes of stock which the Corporation shall have authority to issue is 152,000,000, consisting of 150,000,000 shares of Common Stock, par value $0.001 per share (the "Common Stock") and 2,000,000 shares of Preferred Stock, par value $0.001 per share (the "Preferred Stock")."

4. This Certificate of Amendment of the Corporation's Amended and Restated Certificate of Incorporation has been duly adopted by this Corporation's Board of Directors and stockholders in accordance with the provisions of the Corporation's Amended and Restated Certificate of Incorporation and with Section 242 of the General Corporation Law of the State of Delaware.

IN WITNESS WHEREOF, the undersigned has executed this Certificate of Amendment of Amended and Restated Certificate of Incorporation at Redwood City, California on May 25, 2010.

/s/ Harold E. Selick
Dr. Harold E. Selick
Chief Executive Officer

Exhibit 10.11

[*] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED.

AMENDMENT TO LICENSE AND CO-DEVELOPMENT AGREEMENT

THIS AMENDMENT TO LICENSE AND CO-DEVELOPMENT AGREEMENT (the "**Amendment**") is made and entered into by and between MERCK KGaA, a corporation organized and existing under the laws of Germany and having a principal place of business at Frankfurter Strasse 250, 64293 Darmstadt, Germany (hereinafter referred to as "**Merck**" or **"Licensee"**), and THRESHOLD PHARMACEUTICALS, a corporation organized and existing under the laws of California and having its principal office at 170 Harbor Way, Suite 300, South San Francisco, CA 94080, USA (hereinafter referred to as **"Threshold**" or **"Licensor"**), effective December 2, 2013. Merck and Threshold may each be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, the Parties have entered into a License and Co-Development Agreement dated February 3, 2012 (the "**Agreement**"); and

WHEREAS, the Parties desire to amend the Agreement as set forth herein.

NOW, THEREFORE, in consideration of the mutual promises and covenants set forth below and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

AMENDMENT

1. In the table of Milestone events contained in Section 6.3 of the Agreement, the second row milestone "[*]" is hereby replaced with the following:

   "Enrollment of the 620th patient in the United States Phase III Trial in STS (the "**Additional Milestone**")"

2. Section 12.3 of the Agreement is hereby replaced by:

   "**Termination of the Agreement by Merck for Convenience.** Without limiting Merck's rights under Article 12.2, at any time during the Term, but only after (i) the **[*]** and the **[*]** have occurred, and (ii) **[*]** has occurred, and Merck has paid the corresponding milestone payments and all fees and milestone payments previously accrued, Merck may, at its convenience, terminate this Agreement in its entirety upon ninety (90) days' prior written notice to Licensor."

3. Except as expressly set forth herein, the Agreement remains in full force and effect.

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties have caused this Amendment to be executed and delivered by their respective duly authorized officers as of the day and year first above written, each copy of which shall for all purposes be deemed to be an original.

THRESHOLD

By: /s/ Harold E. Selick
Name: Harold E. Selick, Ph.D.
Title: Chief Executive Officer
Date: 12/17/2013

MERCK KGaA

By: /s/ Axel F. Bengsch
Name: Dr. Axel F. Bengsch
Title: Director, Commercial Business Development, Merck- Serono
Date: 12/02/2013

By: /s/ Simone Heitz
Name: Dr. Simone Heitz
Title: Associate General Counsel
Date: 12/03/2013

[*] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-174844, No. 333-169689, 333-162719 and 333-153475) and Registration Statements on Form S-8 (No. 333-187107, 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 6, 2014, 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, 2013.

/s/ Ernst & Young LLP

San Jose, California
March 6, 2014

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 Annual Report on 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 6, 2014

/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 Annual Report on 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 6, 2014

/s/ JOEL A. FERNANDES
Joel A. Fernandes
Vice President, Finance and Controller
(Principal Financial 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, 2013, 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 6, 2014

/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, 2013, 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 6, 2014

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