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, 2014

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, 2014 was approximately $214,218,509. 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, 2015 there were 71,273,406 shares of the Registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement for the Registrant's 2015 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the Registrant's fiscal year ended December 31, 2014 are incorporated herein by reference into Part III of this Annual Report on Form 10-K.

Threshold Pharmaceuticals, Inc.
TABLE OF CONTENTS

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/or Merck KGaA's ability to commence, conduct and complete, and the timing of the commencement, conduct and completion of clinical trials for our product candidates;
- 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 evofosfamide (formerly 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 our product candidates;
- our and Merck KGaA's ability to timely develop a viable commercial formulation of evofosfamide;
- 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;
- our ability to discover and develop additional product candidates suitable for clinical testing;
- our ability to identify, in-license or otherwise acquire additional product candidates and development programs;
- 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 potential development of new product candidates such as TH-4000 (formerly referred to as PR610 or Hypoxin™), and projected expenditures;
- our ability to complete preclinical and clinical testing successfully for new product candidates, such as TH-4000, 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, evofosfamide (formerly TH-302), is being evaluated in two pivotal Phase 3 clinical trials, one registrational Phase 2 clinical trial, and multiple earlier-stage clinical trials. We have a global license and co-development agreement for evofosfamide with Merck KGaA, Darmstadt, Germany, with an option to co-commercialize in the United States.

Evofosfamide was discovered by our scientists based on our hypoxia-targeted therapeutics prodrug 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 hematological malignancies (also known as cancers of the bone marrow, 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, evofosfamide is designed to remain essentially inactive in normal tissues, but to activate under conditions of tumor hypoxia. Upon activation, evofosfamide 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, evofosfamide may have broad clinical applicability across many types of solid tumors and some hematological malignancies. To explore this broad therapeutic potential of evofosfamide, we are conducting multiple clinical trials to evaluate its safety and efficacy in solid tumors and hematological malignancies in combination with currently marketed anticancer drugs, including traditional chemotherapeutic agents and antiangiogenic agents, and as monotherapy for certain cancers.

We along with our partner Merck KGaA are investigating evofosfamide in the following clinical studies, which are ongoing or recently completed:

Clinical Trial Name	Sponsor*	Therapeutic Area	Combination therapy with evofosfamide	Clinical Stage
TH-CR-406	Threshold	Soft Tissue Sarcoma	doxorubicin	Pivotal Phase 3
MAESTRO	Merck KGaA	Pancreatic Cancer	gemcitabine	Pivotal Phase 3
TH-CR-415	Threshold	n-s NSCLC**	pemetrexed	Registration Phase 2
TH-CR-413	Threshold	Advanced Melanoma	None (evofosfamide monotherapy)	Phase 2
EMR200592-008	Merck KGaA	Soft Tissue Sarcoma	doxorubicin	Phase 2
TH-CR-408	Threshold	Multiple Myeloma	dexamethasone with or without bortezomib	Phase 1/2
EMR200592-006	Merck KGaA	Pancreatic Cancer	gemcitabine and nab-paclitaxel	Phase 1/2
EMR200592-002	Merck KGaA	Solid tumors and Pancreatic Cancer	None (evofosfamide monotherapy) and with gemcitabine	Phase 1 (Japan)
TH-CR-414	Threshold	Advanced Solid Tumors	None (cardiac safety study)	Phase 1
EMR200592-007	Merck KGaA	Advanced Solid Tumors	None (mass balance study)	Phase 1

* Sponsor indicates which company, Threshold or Merck KGaA, is responsible for a particular clinical trial.
**n-s NSCLC=non-squamous non-small cell lung cancer

In addition, evofosfamide is the subject of the following Investigator Sponsored Trials, which are ongoing or recently completed:

Study Sponsor	Therapeutic Area	Combination Therapy with evofosfamide	Clinical Stage
The University of Texas Health Science Center at San Antonio (UTHSCSA)	Glioblastoma	bevacizumab	Phase 1/2
UTHSCSA and Dana Farber Cancer Institute	Glioblastoma	bevacizumab	Phase 2
North Central Cancer Treatment Group	Advanced Kidney Cancer or Liver Cancer	sorafenib	Phase 1
Spanish Task Force in Neuroendocrine Tumors	Pancreatic Neuroendocrine Tumors	sunitinib	Phase 2

We have also licensed worldwide rights to a development program from the University of Auckland based on the clinical-stage oncology compound TH-4000 (formerly referred to as PR610 or Hypoxin™), a hypoxia-targeted epidermal growth factor receptor, or EGFR, tyrosine kinase inhibitor. TH-4000 is designed to selectively release a potent, irreversible tyrosine kinase inhibitor in hypoxic tumors. Preclinical and Phase 1 clinical data suggest that plasma concentrations of TH-4000 that are active in EGFR-dependent tumor xenograft models in mice could be attained in patients with an acceptable therapeutic index. We expect to initiate a Phase 2 proof-of-concept study in a subset of molecularly-defined non-small cell lung cancer patients who we believe may be responsive to TH-4000 in the first half of 2015.

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 evofosfamide successfully.*** We believe that by virtue of targeting tumor hypoxia—a common feature of solid tumors and some hematological malignancies—evofosfamide may have broad clinical applicability across many types of solid tumors and some blood cancers. To maximize the value of evofosfamide, we are conducting clinical trials in therapeutic areas where preclinical and clinical data are supportive of evofosfamide's activity. We are focused on successful execution of clinical and regulatory strategies to support potential submissions for regulatory approval of evofosfamide. We will continue to work on broadening the potential applicability of evofosfamide 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 within tumor tissue, 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 (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. 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.

Evofosfamide Investigational Hypoxia-activated prodrug

The introduction of therapies that preferentially target tumor hypoxia offers the potential to deliver cancer therapies selectively to tumor tissue and to expand the therapeutic options available for cancer patients across the majority of tumor types. To our knowledge, evofosfamide is the most clinically advanced hypoxia-activated prodrug in active development for the treatment of cancer. Evofosfamide 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, evofosfamide 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 evofosfamide 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 evofosfamide will be less likely to produce the systemic toxicity caused by untargeted cytotoxic chemotherapies. Preclinical studies have also shown enhanced antitumor activity of evofosfamide 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 evofosfamide in treating these blood cancers.

Evofosfamide Clinical Development Programs

The development plan for evofosfamide is designed to investigate its safety and efficacy across a broad range of solid tumors and hematologic malignancies. We are developing evofosfamide in areas supported by preclinical and clinical data and where there is high unmet need for new anticancer agents. To date, evofosfamide has been evaluated in more than 1,500 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 evofosfamide monotherapy in patients with advanced solid tumors. We expanded enrollment in this trial to investigate evofosfamide 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 evofosfamide in combination with four currently approved chemotherapies. Data from this collection of clinical trials supported our initial randomized controlled trial of evofosfamide in first-line pancreatic cancer.

The most advanced clinical trials of evofosfamide 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, the 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 evofosfamide orphan drug designation for the treatment of soft tissue sarcoma and pancreatic cancer. The FDA has also granted Fast Track Designation to evofosfamide for the treatment of advanced soft tissue sarcoma. Initiation of these Phase 3 clinical trials was supported by preclinical data in disease-specific models as well as data from Phase 2 clinical trials in the same patient populations. Merck KGaA is conducting additional studies including a Phase 1/2 dose-escalation trial of evofosfamide in combination with gemcitabine and nab-paclitaxel in patients with advanced pancreatic cancer and two studies in Japan: a Phase 2 trial of evofosfamide in combination with doxorubicin in patients with advanced soft tissue sarcoma and a Phase 1 dose-escalation trial of evofosfamide as monotherapy and in combination with gemcitabine in patients with advanced pancreatic cancer.

In 2014, we initiated a 440-patient, randomized, double-blind, placebo-controlled trial of evofosfamide in combination with pemetrexed in patients with advanced non-squamous non-small cell lung cancer (NSCLC). The international Phase 2 trial is designed to compare the combination of evofosfamide and pemetrexed versus the combination of pemetrexed and placebo as second-line therapy in this patient population. In 2013, we also initiated a Phase 2 trial of evofosfamide monotherapy in patients with advanced melanoma. We are also conducting or have completed Phase 1/2 clinical trials of evofosfamide in patients with multiple myeloma and advanced leukemias 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 or completed investigations of evofosfamide in combination with four marketed antiangiogenic agents in multiple Phase 1/2 clinical trials. Threshold and Merck KGaA are conducting two additional Phase 1 trials in patients with advanced solid tumors, one being a cardiac safety study and the other being a mass balance study.

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, evofosfamide.

Evofosfamide pivotal Phase 3 program in soft tissue sarcoma: evofosfamide 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 evofosfamide 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 evofosfamide 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 evofosfamide orphan drug designation for the treatment of advanced soft tissue sarcoma, and the FDA has granted Fast Track Designation to evofosfamide for the treatment of this patient population.

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 evofosfamide with a robust level of statistical significance. The FDA agreed to the amendment under the existing SPA. In December 2013, we announced that the target enrollment of 620 patients was achieved.

In September 2014, we announced that an Independent Data Monitoring Committee, or IDMC, completed the pre-planned interim efficacy and safety analyses of unblinded data from our 406 trial. Based on the IDMC's analyses, which included an assessment of both benefit and risk, the IDMC recommended that the 406 trial should continue as planned to its natural conclusion. We will remain blinded to the data from the 406 trial until the primary analysis of overall survival is conducted, which is scheduled to occur after 434 deaths are reported. We currently project that the required number of events will be reached in the latter half of 2015, with the results of the primary efficacy analysis expected to be available shortly thereafter.

This 406 trial for evofosfamide was initiated following results from a multi-center, dose-escalation Phase 1/2 trial of evofosfamide 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 evofosfamide in combination with full-dose doxorubicin in patients with soft tissue sarcoma followed by evofosfamide maintenance monotherapy for patients who had not progressed after six cycles of combination therapy. Dose-limiting toxicities at an evofosfamide dose of 340 mg/m^2 were Grade 4 thrombocytopenia and Grade 3 infection with Grade 4 neutropenia. The maximum tolerated dose (MTD) of 300 mg/m^2 was established for evofosfamide in combination with the approved dose of 75 mg/m^2 doxorubicin with prophylactic growth factor support. Enrollment was expanded at the MTD, and a total of 91 patients with advanced soft tissue sarcoma previously untreated with systemic chemotherapy were enrolled and treated at the MTD.

Final data from the Phase 2 portion of the 403 trial were published in the September 2, 2014 issue of the *Journal of Clinical Oncology*. The final data included median progression-free survival of 6.5 months (95% confidence interval (CI): 5.8 to 7.7 months); median overall survival of 21.5 months (95% CI 16.0 to 26.2 months); one-year survival of 73% (95% CI: 63% to 81%); two-year survival of 44% (95% CI: 33% to 54%); and overall best response (partial and complete responses, unconfirmed) of 36%.

Development activities in sarcoma planned for 2015: In anticipation of our projection that the required number of events will be reached in the latter half of 2015 with the results of the primary efficacy analysis to be available shortly thereafter, we are focused on activities to prepare for and support the potential submission of marketing applications, assuming the results are supportive.

Evofosfamide 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 evofosfamide in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma. MAESTRO stands for evofosfamide 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 evofosfamide plus gemcitabine compared with placebo plus gemcitabine. In November 2014, we announced that Merck KGaA completed the target enrollment of 660 patients in the trial. 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 evofosfamide 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: evofosfamide at a dose of 240 mg/m^2 plus gemcitabine or evofosfamide at a dose of 340 mg/m^2 plus gemcitabine or gemcitabine alone. If a patient's cancer progressed while on gemcitabine alone, the patient could crossover and be randomized into one of the evofosfamide 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 evofosfamide 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 evofosfamide combinations to gemcitabine alone was 0.61 (95% CI: 0.43 – 0.87), which was highly statistically significant (p=0.005).

Final results of the 404 trial were published in the December 15, 2014 issue of the *Journal of Clinical Oncology* and were consistent with previously-reported results. The final 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 gemcitabine plus evofosfamide (340 mg/ m^2) arm compared with the gemcitabine plus evofosfamide (240 mg/ m^2) and the gemcitabine-alone arms. There was a significant improvement (p=0.008) in progression-free survival associated with a 41% reduction of risk for disease progression or death for patients treated with gemcitabine plus evofosfamide (340 mg/ m^2). This represented a 2.4-month increase in median progression-free survival for patients receiving gemcitabine plus evofosfamide (340 mg/ m^2) compared with gemcitabine alone. The 12-month overall survival rates were also in favor of the gemcitabine plus evofosfamide (340 mg/ m^2) treatment group compared with the control arm (38% vs. 26% (p=0.13)). Median overall survival for gemcitabine, gemcitabine plus evofosfamide (240 mg/ m^2), and gemcitabine plus evofosfamide (340 mg/ m^2) 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 gemcitabine plus evofosfamide treatment arms. In other words, we believe that patients receiving gemcitabine alone who crossed over to receive gemcitabine plus evofosfamide upon disease progression contributed to the survival of the control arm. While not statistically significant, the improvement in median overall survival in the gemcitabine plus evofosfamide treatment arms was consistent with the improvement in median progression-free survival. The most common nonhematologic 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 evofosfamide 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. 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.

In March 2014, we announced that Merck KGaA initiated a Phase 1 dose escalation study assessing the safety, tolerability and anti-tumor activity of evofosfamide in combination with gemcitabine and nab-paclitaxel (Abraxane ®) in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma.

Development activities in pancreatic cancer planned for 2015: Merck KGaA is responsible for conduct and execution of the MAESTRO trial in patients with advanced pancreatic cancer. Currently, we estimate that the protocol-specified events for the MAESTRO trial may be reached in the second half of 2015 with availability of the results of the primary efficacy analysis shortly thereafter. Enrollment is ongoing in the Phase 1/2 trial of evofosfamide in combination with gemcitabine and nab-paclitaxel.

Evofosfamide program in non-squamous non-small cell lung cancer

In July 2014, we announced the initiation of a 440-patient, randomized, double-blind, placebo-controlled trial of evofosfamide in combination with pemetrexed in patients with second-line advanced non-squamous non-small cell lung cancer (which we refer to as the 415 trial). This international Phase 2 trial is designed to support registration and will compare the combination of evofosfamide plus pemetrexed versus the combination of pemetrexed plus placebo as second-line therapy in this patient population. An evofosfamide dose of 400 mg/m^2 will be utilized in combination with full-dose pemetrexed. Overall survival is the primary endpoint; secondary endpoints include safety and assessment of anti-tumor activity as determined by progression-free survival and objective response rate.

Development activities in NSCLC planned for 2015: Enrollment in the trial is expected to continue throughout the year and additional clinical trial sites will be opened.

Evofosfamide program in advanced melanoma

In August 2013, we announced the start of a Phase 2 clinical trial to evaluate the efficacy and safety of evofosfamide 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 evofosfamide therapy. The Phase 2 clinical trial is a single-arm, multi-center study investigating the clinical efficacy and safety of evofosfamide administered at 480 mg/ m^2 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 evofosfamide therapy.

Development activities planned in melanoma for 2015: Enrollment in the trial will continue throughout the year.

Evofosfamide 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 evofosfamide in models of multiple myeloma. *In vitro* studies demonstrated that evofosfamide 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. *I*n *vivo* models of multiple myeloma demonstrated that the combination of evofosfamide 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 evofosfamide in models of leukemia. Evofosfamide 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*, evofosfamide 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 evofosfamide 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 evofosfamide designed to determine the maximum tolerated dose, dose limiting toxicity, safety, tolerability, clinical activity, and pharmacokinetics of evofosfamide in patients with advanced leukemia (which we refer to as the 407 trial). The starting dose of evofosfamide 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 evofosfamide was established at 460 mg/m^2. Early results of this trial suggested activity of evofosfamide 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 evofosfamide 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 evofosfamide. In the first part of the trial, a total of 38 patients received 30-minute bolus administration of evofosfamide at escalating doses of 120—550 mg/ m^2 (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 evofosfamide as a continuous infusion on days 1-5 of a 21-day cycle. Two of three patients treated with continuous infusion of evofosfamide (460 mg/ m^2/day) experienced dose-limiting toxicities of Grade 3 mucositis or Grade 3 hyperbilirubinemia; continuous administration maximum-tolerated dose was established at 330 mg/ m^2/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/ m^2 bolus evofosfamide had complete resolution of leukemia cutis. One AML patient at 550 mg/ m^2 bolus evofosfamide had a complete response with incomplete platelet recovery (CRp), and one AML patient at 440 mg/ m^2 bolus evofosfamide had a complete response.

Development activities planned in leukemia for 2015: The 407 trial was completed and all patients discontinued treatment. Evaluation of evofosfamide in combination with other chemotherapies for the treatment of advanced leukemias is under consideration.

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 evofosfamide to determine the maximum tolerated dose, dose limiting toxicity, safety, tolerability, clinical activity, and pharmacokinetics of evofosfamide and dexamethasone with and without bortezomib (Velcade®), a proteasome inhibitor, in patients with relapsed/refractory multiple myeloma (which we refer to as the 408 trial). The study has three parts designed to establish the maximum tolerated dose of evofosfamide in combination with dexamethasone (Part A), (evaluate the combination of evofosfamide with dexamethasone at the established maximum tolerated dose (Part B), and evaluate the combination of evofosfamide and dexamethasone with bortezomib, currently used to treat patients with multiple myeloma) (Part C).

The dose of evofosfamide administered in the Part A dose escalation portion of the study was 240, 340, or 480 mg/ m^2 (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 evofosfamide. As presented at the annual meeting of the American Society of Hematology (ASH) in December 2013, the maximum tolerated dose of evofosfamide was established at 340 mg/ m^2. Dose-limiting toxicities of Grade 3 stomatitis were reported during the first treatment cycle for the first two patients treated at 480 mg/m^2 evofosfamide; therefore, the maximum tolerated dose of evofosfamide was established at 340 mg/m^2. In May 2014, preliminary results were presented at the annual meeting of the American Society for Clinical Oncology (ASCO) on data from 24 patients in the dose-escalation and dose-expansion portions of the study who initiated treatment prior to March 1, 2014; analyses reflected the clinical database as of May 19, 2014. Of these 24 patients, 17 were treated at the maximum tolerated dose of evofosfamide. Patients had received a median of 6.5 systemic therapies prior to enrollment. The most common adverse events related to evofosfamide occurring in at least 25% of patients were nausea and fatigue. The most common Grade 3/4 hematologic adverse events related to evofosfamide were thrombocytopenia (29%) and leukopenia (25%). Of the 24 patients included in the ASCO presentation, 23 were evaluable for response. According to modified International Myeloma Working Group (IMWG) criteria, best responses included four partial responses (4 PR), two minimal responses (2 MR), and 15 stable disease (15 SD) assessments; two patients had progressive disease (2 PD). The clinical benefit rate for patients treated at the maximum tolerated dose of evofosfamide (n=16 evaluable patients) was 31% (comprised of 3 PR and 2 MR).

In July 2014, we announced initiation of the third and final part of the trial designed to investigate evofosfamide in combination with the proteasome inhibitor bortezomib (Velcade®) and low-dose dexamethasone. In December 2014, preliminary results from this portion of the trial were reported at the 56th ASH Annual Meeting and Exposition, or ASH 2014. At ASH 2014, preliminary safety and efficacy analyses from 9 patients were presented. The recommended Phase 2 dose of evofosfamide was established at 340 mg/m^2 and no dose limiting toxicities were observed in the 6 patients treated at this dose level. Safety data were available for 8 of 9 patients. The most common Grade 3/4 hematological adverse events were thrombocytopenia (reported in 4 patients), anemia (reported in 2 patients), and lymphopenia (reported in 2 patients). Fatigue (reported in 5 patients; one Grade 3/4) and nausea (reported in 4 patients; one Grade 3/4) were the most common non-hematological adverse events. Five serious adverse events (SAEs) were reported in 4 patients. One SAE of thrombocytopenia was considered related to evofosfamide. Skin toxicity, an adverse event of interest with evofosfamide, was limited: a Grade 2 rash resulting in treatment delay was reported at the 240 mg/m^2 dose of evofosfamide, and one Grade 2 skin lesion with no impact on treatment was reported at the 340 mg/m^2 dose of evofosfamide. Based on IMWG criteria and our preliminary assessment of clinical activity, partial responses (one very good partial response and one partial response) were observed in 2 of 7 (29%) evaluable patients overall and 2 of 4 (50%) evaluable patients at the recommended Phase 2 dose of evofosfamide.

Development activities planned in multiple myeloma for 2015: We plan to enroll up to 24 patients at the maximum tolerated dose of evofosfamide (340 mg/ m^2) in combination with bortezomib and low-dose dexamethasone and expect to present preliminary findings at a medical conference in 2015.

Evofosfamide 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 evofosfamide is designed to be selectively activated under conditions of severe tumor hypoxia, the combination of evofosfamide with antiangiogenic therapy has the potential to be an effective anticancer treatment. Preclinical models demonstrated enhanced antitumor activity of evofosfamide 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, evofosfamide has been or is expected to be investigated in combination with antiangiogenic therapies in a variety of tumor types in human clinical trials. Current studies include the following:

- TH-CR-410: A Threshold sponsored Phase 1 trial evaluating the safety of evofosfamide in combination with sunitinib in patients with advanced renal cell carcinoma (RCC), gastrointestinal stromal tumors (GIST), and pancreatic neuroendocrine tumors (pNET). All patients have completed the study.
- EMR 200592-012: A Phase 2 trial to assess the activity and safety of evofosfamide in combination with sunitinib in patients with well- and moderately-differentiated metastatic pancreatic neuroendocrine tumors (pNET) that are naïve to systemic treatment.

- TH-IST-4003: A Phase 1/2 Investigator Sponsored Trial evaluating the safety and efficacy of evofosfamide in combination with bevacizumab in patients with recurrent glioblastoma following bevacizumab failure.
- TH-IST-4008: A Phase 2 FDA-funded Investigator Sponsored Trial evaluating the safety and efficacy of evofosfamide in combination with bevacizumab in patients with recurrent glioblastoma following bevacizumab failure.
- TH-IST-4001: A Phase 1 Investigator Sponsored Trial evaluating the safety of evofosfamide in combination with pazopanib in patients with advanced solid tumors.
- TH-IST-4004: A Phase 1/2 Investigator Sponsored Trial of evofosfamide in combination with sorafenib in patients with advanced kidney cancer or liver cancer that cannot be removed by surgery.

TH-CR-410 Phase 1 dose escalation trial of evofosfamide 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 evofosfamide (240 mg/ m^2 to 480 mg/ m^2) 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/ m^2. One of 6 evaluable patients treated at 340 mg/ m^2 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.

Status: Enrollment in this trial has been completed, and all patients have discontinued from the trial. The recommended Phase 2 dose of evofosfamide (480 mg/ m^2) was established and will be evaluated further in an Investigator Sponsored Trial of evofosfamide in combination with sunitinib in patients with pancreatic neuroendocrine tumors (pNET) (see below).

EMR 200592-012: A Phase 2 trial of evofosfamide in combination with sunitinib in patients with pNET

The -012 trial is an Investigator-Sponsored Phase 2 trial designed to assess the activity and safety of evofosfamide in combination with sunitinib in patients with well- and moderately-differentiated metastatic pancreatic neuroendocrine tumors (pNET) who are naïve to systemic treatment. The study is being sponsored by the Spanish Task Force in Neuroendocrine Tumors.

Status: Enrollment in this Investigator Sponsored Trial is expected to commence in 2015.

TH-IST-4003: Phase 1/2 trial of evofosfamide *and bevacizumab in patients with glioblastoma (GBM) following bevacizumab failure*

The 4003 trial is a U.S. investigator-sponsored Phase 1/2 clinical trial evaluating evofosfamide in combination with Avastin® (bevacizumab) in patients with recurrent glioblastoma (GBM) following bevacizumab failure. Surgical resection followed by concomitant radiotherapy and chemotherapy is the standard of care for patients with newly-diagnosed GBM. Single-agent bevacizumab is the only FDA-approved therapy for GBM patients with progressive disease following prior therapy. After disease progression on bevacizumab, patients may start a subsequent bevacizumab-containing regimen.

Preliminary results from the 4003 trial were reported at the ESMO 2012 Congress, the 2013 Scientific Meeting and Education Day of the Society for Neuro-Oncology (SNO), and most recently at SNO in November 2014. As reported by Andrew J. Brenner, M.D., Ph.D., the study principal investigator at SNO 2014, a total of 23 patients in the Phase 1/2 study were treated with bevacizumab 10 mg/kg every two weeks and evofosfamide dose escalated 240 – 670 mg/m^2 every two weeks (four-week cycle) until disease progression. Patients had received a median of three prior systemic anticancer regimens including both chemoradiation and bevacizumab. No Grade 4 adverse events were observed. Three Grade 3 adverse events in three patients were observed: skin ulceration at 340 mg/m^2, thrombocytopenia at 670 mg/m^2, and oral mucositis at 670 mg/m^2. Primary evofosfamide-related toxicities were mucosal, but were not dose-limiting: rectal mucositis in one of four (1/4) patients at 480 mg/m^2 and all patients (13/13) at 670 mg/m^2 (all Grade 1 or 2). Oral mucositis was less frequent. Best tumor responses in 22 patients evaluable by Response Assessment in Neuro-Oncology (RANO) criteria included one complete response and three partial responses for a response rate of 18%, and ten stable disease assessments for a clinical benefit rate of 64%; eight patients had progressive disease. Median progression-free survival was 2.8 months (95% confidential interval (CI): 1.9 to 3.9 months) and 4-month progression-free survival was 22% (95% CI: 3.2% to 41%). Median overall survival was 4.6 months (95% CI: 3.4 to 6.2 months).

Status: Enrollment has been completed in this investigator-sponsored trial, and the recommended Phase 2 dose of evofosfamide was established at 670 mg/ m^2 in combination with 10 mg/kg bevacizumab administered every other week. In 2014, the investigator received funding from the FDA to conduct a multiple-center Phase 2 trial of evofosfamide at the recommended Phase 2 dose in combination with bevacizumab in this patient population, as described below.

TH-IST-4008: *FDA-funded Phase 2 Investigator Sponsored Trial in GBM*

In September 2014, the FDA, through its Office of Orphan Product Development, awarded Dr. Brenner a grant for a Phase 2 clinical trial of evofosfamide for the treatment of GBM, which we refer to as TH-IST-4008. Dr. Brenner's planned investigator-sponsored Phase 2 trial, which is designed to assess safety and efficacy of 670 mg/m^2 evofosfamide in combination with bevacizumab for the treatment of recurrent GBM following prior bevacizumab failure, is expected to enroll up to 33 patients. PET imaging will also be conducted in an effort to predict which patients may benefit from evofosfamide combination therapy. Dana Farber Cancer Institute and The University of Texas at Austin will participate in the trial.

Status: Enrollment in this Investigator Sponsored Trial is planned to begin in the first half of 2015.

TH-IST-4001: Phase 1 dose escalation trial of evofosfamide and pazopanib in patients with advanced solid tumors

The 4001 trial evaluated evofosfamide 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 ≥ 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 Investigator Sponsored Trial has completed enrollment. There are no current plans for further investigation of evofosfamide in combination with pazopanib at this time.

TH-IST-4004: A Phase 1/2 Investigator Sponsored Trial of evofosfamide in combination with sorafenib in patients with advanced kidney cancer or hepatocellular cancer

Study 4004 is a Phase 1/2 Investigator Sponsored Trial designed to evaluate the safety and efficacy of evofosfamide in combination with sorafenib (Sutent®)) in patients with advanced kidney cancer or liver cancer that cannot be removed by surgery. The primary objectives of the Phase 1 portion are to determine the maximum-tolerated dose and recommended Phase 2 dosing for the combination of sorafenib and evofosfamide; overall response rate in patients with advanced hepatocellular cancer will be assessed in the Phase 2 portion.

Status: This Investigator Sponsored Trial is currently enrolling patients in the Phase 1 portion of the study.

TH-4000 Investigational Hypoxia-Activated EGFR Tyrosine Kinase Inhibitor

In September 2014, we licensed worldwide rights to a development program from the University of Auckland based on the clinical-stage oncology compound TH-4000 (formerly referred to as PR610 or Hypoxin™), a hypoxia-activated epidermal growth factor receptor, or EGFR, tyrosine-kinase inhibitor (TKI). TH-4000 is designed to selectively release a potent, irreversible EGFR-TKI in hypoxic tumors. Preclinical and Phase 1 clinical data suggest that plasma concentrations of TH-4000 that are active in EGFR-dependent tumor xenograft models in mice could be attained in patients with an acceptable therapeutic index. We expect to initiate a Phase 2 proof-of-concept study in a subset of molecularly-defined non-small cell lung cancer patients who we believe may be responsive to TH-4000 in the first half of 2015.

[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 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 evofosfamide 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 evofosfamide 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 evofosfamide 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 835,000 per annum.

The table below depicts the latest estimates from the American Cancer Society on expected 2015 incidence and deaths for cancers in the United States that we consider therapeutic areas of interest for evofosfamide.

Type of Cancer	New Cases	Deaths
Prostate cancer	220,800	27,540
Lung cancer	221,200	158,040
Melanoma	73,870	9,940
Kidney and Renal Pelvis	61,560	14,080
Head and Neck	59,340	12,290
Leukemia (all)	54,270	24,450
Pancreatic cancer	48,960	40,560
Liver (& intrahepatic bile duct)	33,660	24,550
Brain (& other nervous system)	22,850	15,320
Myeloma	26,850	11,240
Soft tissue sarcoma (including heart)	11,930	4,870

The market opportunity for our two most advanced clinical development programs with evofosfamide 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. There are approximately 35,000 new cases of soft tissue sarcoma in the U.S. and European Union per annum.

Pancreatic Cancer

It is estimated that 337,872 cases of pancreatic cancer are diagnosed worldwide every year, accounting for 2.4% of all cancers.Almost 67% of cases are diagnosed in people aged 65 and over; it is uncommon in people under the age of 45. Pancreatic cancer has a low survival rate regardless of stage of disease, with 93% of patients dying from their disease within 5 years. It is estimated that there are 330,372 deaths from pancreatic cancer worldwide 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 complete enrollment in 2016.

Discovery Research

We have research programs focused on better understanding the mechanism and maximizing the effectiveness of evofosfamide 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. Evofosfamide 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 evofosfamide 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 evofosfamide. Under our license and co-development agreement with Merck KGaA, Merck KGaA has exclusive rights to manufacture evofosfamide for clinical and commercial use, except that we have the right to obtain clinical supply of evofosfamide for clinical trials for United States approval of evofosfamide 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 evofosfamide API and evofosfamide drug product to meet our and Merck KGaA's clinical supply needs of evofosfamide. We have no long-term commitments or commercial supply agreements with any of our evofosfamide suppliers.

While we have developed plans to meet our and Merck KGaA's clinical supply needs for our ongoing clinical trials of evofosfamide, 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 evofosfamide API and drug product manufactured, or if manufacturing is interrupted at our single source contract manufacturers for evofosfamide API and evofosfamide 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 evofosfamide clinical program. In any event, additional agreements for more supplies of each of our product candidates, including evofosfamide, 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 evofosfamide 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 evofosfamide 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 evofosfamide or increase the manufacturing capacity for evofosfamide or any of our other product candidates in a timely or economically feasible manner.

We also expect to rely on contract manufacturers or other third parties to produce sufficient quantities of clinical trial product for any other product candidates that we may develop. In this regard, while we have obtained certain quantities of TH-4000 API and drug product from our licensor, we may determine that such API and drug product is not usable or is otherwise insufficient in order for us to commence or complete our planned Phase 2 proof-of-concept study of TH-4000 and we may need to obtain sufficient supplies of TH-4000 API and drug product from contract manufacturers prior to commencing our planned Phase 2 proof-of-concept study, which could delay the commencement or completion of the planned study, could increase our costs and could negatively impact our planned TH-4000 development program. Depending upon the duration of the clinical studies, we might need to develop a new formulation of TH-4000. It is possible that we might not be able to develop a formulation with adequate quality that meets the need for testing in our clinical trials. In any event, in order for us to commence any planned or potential future clinical trials of our product candidates, we need to obtain or have manufactured sufficient quantities of clinical trial product and there can be no assurance that we will be able to obtain sufficient quantities of clinical trial product in a timely manner or at all.

Research and Development Expenses

During the years ended December 31, 2014, 2013 and 2012, we spent $35.8 million, $29.3 million and $18.8 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 evofosfamide 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 evofosfamide in the United States. To date we have received upfront and milestone payments of $110 million. 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 evofosfamide in the soft tissue sarcoma indication. We and Merck KGaA will jointly develop evofosfamide in all other cancer indications being pursued. Merck KGaA will pay 70% of worldwide development costs for evofosfamide. Subject to FDA approval in the United States, Merck KGaA will initially be responsible for commercialization of evofosfamide 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 evofosfamide in the United States. Additionally, we retain the option to co-commercialize evofosfamide 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 evofosfamide 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 evofosfamide in such country or ten years following the commercial launch of a product containing evofosfamide 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 the University of Auckland

On September 23, 2014, we entered into an exclusive license agreement with Auckland UniServices Ltd., a wholly-owned company of the University of Auckland. Pursuant to the agreement, we licensed exclusive worldwide rights to a development program based on TH-4000 from the University of Auckland. We expect to initiate a Phase 2 proof-of-concept study in a subset of molecularly-defined non-small cell lung cancer patients who we believe may be responsive to TH-4000 in the first half of 2015. Under the terms of this agreement, we made no upfront payment but we are required to pay all costs of development, as well as annual license maintenance fees starting in 2017, and assuming that we determine to advance the clinical development of TH-4000 beyond our planned Phase 2 proof-of-concept study, we would be required to pay development, regulatory and sales-based milestone payments and royalties on net sales of products, including TH-4000, incorporating technology licensed from the University of Auckland.

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 25, 2015, we owned 107 U.S. and foreign patents and patent applications relating to evofosfamide 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 and one of which is co-owned with Merck KGaA. These include 7 issued U.S. patents expiring from 2024 to 2031 and 28 issued foreign patents expiring from 2024 to 2027 (in each case, without including any regulatory-delay based patent term extension), as well as 13 pending U.S., 1 pending Patent Cooperation Treaty and 58 pending foreign national patent applications, which, if issued, would in each case expire from 2024 to 2035 (without including any regulatory- or patent office-delay based patent term extension).

As of February 25, 2015, we have rights to 39 U.S. and foreign patents and patent applications relating to TH-4000 and its manufacture, formulation and use, each of which are exclusively licensed by us from Auckland Uniservices Ltd. These include 4 issued foreign patents expiring in 2030, as well as 3 pending U.S., and 32 pending foreign national patent applications, which, if issued, would in each case expire from 2030 to 2035 (without including any regulatory- or patent office-delay based patent term extension).

Although we have U.S. and foreign issued patents that cover certain hypoxia-targeted prodrugs, including evofosfamide and TH-4000, 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. If we are not able to obtain adequate protection for, or defend, the intellectual property position of evofosfamide, TH-4000 or any other potential future product candidates, then we may not be able to retain or attract collaborators to partner our development programs. Further, even if we can obtain protection for and defend the intellectual property position of evofosfamide, TH-4000 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, Auckland Uniservices Ltd., and potential future collaborators may not generate any revenues or profits from evofosfamide, TH-4000 or any potential future product candidates or our revenue or profit potential would be significantly diminished.

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 evofosfamide 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 evofosfamide. 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 evofosfamide.

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, evofosfamide would compete with Gemzar®, marketed by Eli Lilly and Company; Tarceva®, marketed by Roche/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, evofosfamide could potentially compete with doxorubicin or the combination of doxorubicin and ifosfamide, generic products sold by many manufacturers. If approved for commercial sale for treatment-resistant non-small cell lung cancer, TH-4000 could potentially compete with other EGFR-TKIs currently in late-stage clinical development including AstraZeneca's AZD-9291, Clovis Oncology's CO-1686, and Pfizer's dacomitinib.

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 become effective before human clinical trials may commence. The IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA requests an extension or raises concerns about the conduct of the clinical trials as outlined in the application. If the FDA has any concerns, the sponsor of the application and the FDA must resolve the concerns before 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. Investigator Sponsored Trials are INDs held by investigators that utilize investigational drugs supplied by a pharmaceutical manufacturer. Data generated under Investigator Sponsored Trials may not be as robust as commercially sponsored IND trials. 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. [18F]-HX4 [flortanidazole (18F)] will require submission of a separate IND.

Clinical Trials

Clinical trials for new drug candidates are typically conducted in three sequential phases, under Good Clinical Practices, 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. Risk Evaluation and Mitigation Strategies, or REMS, may be required for approval of an NDA. Even if such data or REMS 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.

Other Health Care Laws

In addition to FDA restrictions, other federal and state laws restrict our business practices. In the United States, we are subject to various federal and state laws pertaining to healthcare, including, without limitation, "fraud and abuse" laws such as anti-kickback and false claims laws, data privacy and security laws, and payment transparency 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, among other things, 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 penalties, civil money penalties, and exclusion from participation in federal healthcare 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.

Civil and Criminal false claims laws and civil monetary penalties laws prohibit, among other things, any person or entity 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 civil False Claims Act in connection with their off-label promotion of drugs. Penalties for a violation of the civil False Claims Act, some of which may be broader in scope, 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 civil 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 substantial penalties, including, for example, potentially significant fines which may cause a decline in our stock price.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information

Additionally, the federal Physician Payments Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, collectively the ACA, and its implementing regulations, require certain manufacturers of drugs, devices, biological products and medical supplies to report annually information related to certain payments or other transfers of value provided to physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

In addition, many states have adopted laws similar to the aforementioned laws. Some of these state prohibitions may be broader in scope and may apply to referral of patients for healthcare services reimbursed by any source, not only the Medicare and Medicaid programs. Additionally, our business operations in foreign countries and jurisdictions may subject us to additional regulation.

If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal and civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

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.

Revenues and Information About Geographic Areas

All of our revenues for the years ended December 31, 2014, 2013, 2012 resulted from the amortization of upfront and milestone payments received under our collaboration with Merck KGaA. Further information on our collaboration with Merck KGaA is included in Note 3 to our consolidated financial statements. All of our long-lived assets are maintained in the United States.

Employees

As of December 31, 2014, we had 61 employees, including 20 who hold Ph.D. and/or M.D. degrees. 48 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 evofosfamide (formerly 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 evofosfamide, our ability to generate revenue from product sales will be significantly delayed.

We have focused our development activities on evofosfamide, and we do not presently have any other compounds in clinical development. Substantially all of our efforts and expenditures over the next few years are expected to be devoted to evofosfamide. Accordingly, our future prospects are substantially dependent on the successful development, regulatory approval and commercialization of evofosfamide. In addition, in February 2012, we entered into a global license and co-development agreement for evofosfamide 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 evofosfamide. In addition, evofosfamide is not expected to be commercially available in the near term, if at all. Further, the commercial success of evofosfamide 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 evofosfamide, 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 evofosfamide to achieve successful clinical trial endpoints, delays in clinical trial enrollment or events or in the clinical development of evofosfamide generally, unanticipated adverse side effects related to evofosfamide or any other adverse developments or information related to evofosfamide would significantly harm our business, our prospects and the value of our common stock. Evofosfamide 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 evofosfamide in combination with doxorubicin versus doxorubicin alone in patients with soft tissue sarcoma, and the MAESTRO trial of evofosfamide in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma, being conducted by Merck KGaA. 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 such trial or conduct additional clinical trials. Even if we believe that the data from required Phase 3 clinical trials are positive, the FDA could require additional trials or other testing before approving evofosfamide 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 evofosfamide. 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 evofosfamide, 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 evofosfamide 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 evofosfamide would be limited.

Although we have obtained agreement with the FDA on an SPA for our pivotal Phase 3 clinical trial of evofosfamide in combination with doxorubicin versus doxorubicin alone in patients with soft tissue sarcoma and Merck KGaA has obtained agreement with the FDA on an SPA for the pivotal Phase 3 clinical trial of evofosfamide 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 evofosfamide. Merck KGaA has also obtained an agreement with the FDA on an SPA for the MAESTRO trial of evofosfamide. 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 evofosfamide 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 or Merck KGaA may propose to our respective protocols 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 from the 406 trial or the MAESTRO trial will be found to be adequate to support an efficacy claim and product approval. Therefore, despite the potential benefits of SPA agreements, significant uncertainty remains regarding the clinical development of and regulatory approval process for evofosfamide and it is possible that we and Merck KGaA might never receive any regulatory approvals for evofosfamide.

Preclinical studies and Phase 1 or 2 clinical trials of our product candidates may not predict the results of subsequent human clinical trials.

Preclinical studies, including studies of our product candidates in animal models of disease, may not accurately predict the results of human clinical trials of those product candidates. In particular, promising animal studies suggesting the efficacy of evofosfamide for the treatment of different types of cancer may not accurately predict the ability of evofosfamide to treat cancer effectively in humans. Likewise preclinical and Phase 1 clinical data that suggest that plasma concentrations of TH-4000 that are active in tumor xenograft models in mice could be attained in patients may not accurately predict whether a safe and effective dose can be attained in humans. Evofosfamide, TH-4000 or any other compounds we may develop 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 product 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. Initial results from Phase 1 and Phase 2 clinical trials of evofosfamide also may not be confirmed by later analysis or in subsequent larger clinical trials, including in the 406 trial the 415 trial and the MAESTRO trial. In particular, the results that achieved the primary endpoint for progression-free survival in the Phase 2b trial of evofosfamide 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. Likewise, the results in the Phase 1/2 trial of evofosfamide in patients with soft tissue sarcoma may not predict the results of overall survival for patients in the same study or subsequent studies, including in the 406 trial. As a result, despite the results reported in earlier clinical trials for evofosfamide, 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 evofosfamide. Our and Merck KGaA's failure to successfully complete clinical trials and obtain regulatory approval for evofosfamide 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 evofosfamide.

Our success in developing, manufacturing and commercializing evofosfamide depends on our relationship with Merck KGaA. On February 3, 2012, we entered into a global license and co-development agreement for evofosfamide 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 evofosfamide in the soft tissue sarcoma indication. We and Merck KGaA will jointly develop evofosfamide in all other cancer indications being pursued. We have rights to co-promote evofosfamide in the United States, which we can exercise by giving notice during specified periods, and have the right to co-commercialize evofosfamide 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 evofosfamide;
- 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 evofosfamide;
- Merck KGaA may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial or abandon evofosfamide, repeat or conduct new clinical trials or require a new formulation of evofosfamide 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 evofosfamide in the United States if we chose to do so, or our reliance on Merck KGaA to promote evofosfamide in the United States;
- our inability to co-promote or co-commercialize evofosfamide in any country outside the United States, which makes us solely dependent on Merck KGaA to promote and commercialize evofosfamide in foreign countries;
- if evofosfamide is approved for commercial sale and we exercise our co-promotion or co-commercialization rights for evofosfamide 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 evofosfamide, including federal and state reporting requirements;
- 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 evofosfamide 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 evofosfamide and we may be unable to obtain any remedy against Merck KGaA if they fail to do so, or to 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 evofosfamide 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 evofosfamide 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 evofosfamide 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 evofosfamide 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 evofosfamide. 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 evofosfamide; if we cease funding development of evofosfamide under the collaboration agreement, then we will be entitled to receive a royalty, but will lose our right to co-commercialize evofosfamide and share in profits, which could substantially harm our business, financial condition and prospects.

Merck KGaA has the right to terminate the agreement on 90 days' prior written notice, or following our uncured material breach. If Merck KGaA terminates the agreement at its election, then we would become responsible for the costs of development and commercialization of evofosfamide, and there can be no assurance we would be able to do fund those costs, or to find another collaborator for the continued development and commercialization of evofosfamide. If we are unable to maintain our collaborative relationship with Merck KGaA, we may be unable to continue development, manufacturing and any marketing activities for evofosfamide at our own expense.

Even if we were able to continue these activities at our expense, this would significantly increase our capital and infrastructure requirements, would necessarily impose delays on our evofosfamide development program, may limit the indications we are able to pursue and could prevent us from effectively developing and commercializing evofosfamide. 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 evofosfamide, 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 evofosfamide and we may lack the capital and resources necessary to develop evofosfamide alone. Disputes with Merck KGaA may delay or prevent us from further developing, manufacturing or commercializing evofosfamide, 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 obtain regulatory approval and commercialize our product candidates.

Delays in 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.

For example, we previously projected that the number of events, or deaths, required for the primary efficacy analysis of the 406 trial may be reached by mid-2015; however, based on projections derived from the interim analyses of both efficacy and safety data from the 406 trial conducted by the IDMC in 2014 that suggested that event rates in the 406 trial were slower than expected, we currently project that the required number of events will be reached in the latter half of 2015, with overall survival results expected to be available soon thereafter. However, because the timing of the availability of the overall survival results of the 406 trial is event-driven, which we do not control, we cannot predict with certainty when overall survival results will be available and it is possible that the completion of the 406 trial could again be delayed beyond our expectations.

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 and/or Merck KGaA 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 and/or Merck KGaA can obtain regulatory approval for a product candidate, we and/or Merck KGaA 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 our or Merck KGaA successfully completing clinical testing within the time frames we have planned or anticipated, or at all. We or Merck KGaA may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us or Merck KGaA from receiving regulatory approval or commercializing our product candidates, including the following:

- our or Merck KGaA's clinical trials may produce negative or inconclusive results, and we or Merck KGaA may decide, or regulators may require us and Merck KGaA, 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 clinical trials for our product candidates may be slower than we anticipate, resulting in significant delays and additional expense;
- we, or Merck KGaA 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 our product candidates, during a clinical trial could cause the trial to be terminated or require additional studies. Furthermore, some of our clinical trials are overseen by IDMCs or Data and Safety Monitoring Boards, or DSMBs. 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 periodic review of, unblinded data. Any of our ongoing clinical trials overseen by an IDMC or DSMB may be discontinued or amended in response to recommendations made by responsible IDMCs or DSMBs based on their review of trial results and an IDMC or DSMB 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 conducted pre-planned interim efficacy and safety analyses of unblinded data for the 406 trial in September 2014 and recommended that the 406 trial should continue as planned to its natural conclusion. The IDMC also monitors patient safety in the 406 trial on an ongoing basis. 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. The recommended termination or modification of any of our or Merck KGaA's ongoing late-stage clinical trials by an IDMC or DSMB, including the 406 trial, could materially and adversely impact the future development of evofosfamide, 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 and Merck KGaA 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 or Merck KGaA 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 evofosfamide, 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 are expected to have undesirable side effects. For example, in clinical trials of evofosfamide, 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 or Merck KGaA's 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, our product candidates may prove to have undesirable or unintended side effects or other characteristics adversely affecting their safety, efficacy or cost effectiveness that could prevent or limit their approval for marketing and successful commercial use, or that could delay or prevent the commencement and/or completion of clinical trials for our product candidates.

We have not yet gained sufficient experience with a commercial formulation of evofosfamide.

The formulation of evofosfamide that we and Merck KGaA are using in our clinical trials was changed to address issues with a prior formulation that was subject to storage and handling requirements that were not suitable for a commercial product. The current formulation of evofosfamide 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 evofosfamide, then we and/or Merck KGaA may be required to repeat some or all of our respective Phase 3 clinical trials of evofosfamide, 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 evofosfamide.

The initial clinical formulations developed for TH-4000 and our potential future product candidates may not remain stable throughout the clinical testing phase.

We have limited experience and data on the drug substance synthesis and the initial formulation for TH-4000. This initial formulation and those of our potential future product candidates may not remain stable during the clinical testing phase. If these formulations were found to be unstable during clinical testing, we may be required to repeat the initial clinical trials which could increase our costs and delay the development of the applicable product candidate. We may be required to reformulate these product candidates, including TH-4000, to improve stability. However, it is possible that we might not be able to develop a formulation of TH-4000 or other future product candidate with adequate quality that meets the need for testing in our clinical trials. We may also be required to perform additional clinical bridging studies which may further delay development. We may also be unable to scale up the manufacturing process to synthesize the current drug substance and current formulations, or the newly developed formulations, any of which could adversely affect our ability to advance the development of, and potentially obtain regulatory approval of, the applicable product candidate.

Even though we and Merck KGaA have received orphan drug designation for evofosfamide, we may not receive orphan drug marketing exclusivity for evofosfamide. 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 evofosfamide for the treatment of soft tissue sarcoma and pancreatic cancer in the United States and the European Union or EU. 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 U.S. 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 evofosfamide, 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 evofosfamide 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 evofosfamide, which could create a more competitive market for us and/or Merck KGaA.

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 evofosfamide 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.

The "fast track" designation for development of any of our product candidates may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood the product candidate will receive regulatory approval.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA "fast track" designation for a particular indication. Marketing applications filed by sponsors of product candidates in the fast track process may qualify for priority review under the policies and procedures offered by the FDA, but the fast track designation does not assure any such review. Although we have obtained a fast track designation from the FDA for evofosfamide for the treatment of previously untreated patients with metastatic or locally advanced unresectable soft tissue sarcoma, receipt of fast track designation does not ensure in a faster development process, review or FDA approval. In addition, the FDA may withdraw our fast track designation at any time. If we lose our fast track designation for evofosfamide, the approval process may be delayed. In addition, our fast track designation does not guarantee that we will be able to take advantage of the expedited review procedures and does not increase the likelihood that evofosfamide will receive any regulatory approvals.

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 discover and develop additional prodrug product candidates suitable for clinical testing, and we also may not be able to successfully acquire or in-license and develop additional prodrug product candidates or programs, either of 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, evofosfamide is currently our only product candidate in clinical development and we may be unable to discover and develop additional product candidates suitable for clinical testing. Likewise our strategy may include acquiring or in-licensing additional product candidates or development programs that build on our expertise and complement our pipeline. Any growth through acquisition or in-licensing will depend upon the availability of suitable product candidates at favorable prices and upon advantageous terms and conditions. Even if appropriate acquisition or in-licensing opportunities are available, we may not have the financial resources necessary to pursue them. In addition, other companies, many of which may have substantially greater financial, marketing and sales resources, compete with us for acquisition or in-licensing opportunities. In addition, we may not be able to realize the anticipated benefits of any acquisition or in-licensing opportunity for a variety of reasons, including the possibility that a product candidate proves not to be safe or effective in later clinical trials or the integration of an acquired or licensed product candidate gives rise to unforeseen difficulties and expenditures. For example, in the fourth quarter of 2014, we licensed rights to TH-4000, a clinical-stage investigational compound that we plan to evaluate in a Phase 2 proof-of-concept study in a population of patients with non-small cell lung cancer. However, our evaluation of TH-4000 is at an early stage and it is possible that TH-4000 may not be found to be safe or effective in the planned Phase 2 proof-of-concept study or in any other studies that we may conduct, and we may otherwise fail to realize the anticipated benefits of our licensing of this product candidate. In this regard, TH-4000 was previously being developed in a different patient population than we are targeting and a prior clinical trial evaluating TH-4000 in that patient population was terminated prematurely due to unacceptable toxicity. While we plan to evaluate TH-4000 in a patient population that we believe may be responsive to TH-4000 at doses lower than was targeted in the terminated clinical trial, we cannot assure you that we will be able to determine an appropriate dose that is both safe and effective for the patient population we are targeting. In any event, any growth through development of additional product candidates will depend upon our discovering and/or identifying and obtaining product candidates, our ability to develop those product candidates and the availability of funding to complete the development of, obtain regulatory approval for and commercialize these product candidates. If we are unable to discover or obtain suitable product candidates for development, 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 and /or Merck KGaA 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 and/or Merck KGaA obtain regulatory approval for evofosfamide, we and/or Merck KGaA 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 evofosfamide, 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 any approved products for off-label uses could also subject us to false claims litigation under federal and state statutes, which could lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which we promote or distribute any approved 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 any 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 evofosfamide. 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 evofosfamide, 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, 2014, we had an operating loss of $31.3 million and a net loss of $21.6 million, including $9.3 million in non-cash income related to the change in the fair value of outstanding warrants. 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 co-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 product candidates 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 evofosfamide are expected to be funded by Merck KGaA, we expect that we will need to raise additional capital to complete the clinical development of evofosfamide, to develop our recently licensed TH-4000 product candidate, and to support new in-house development programs or to in-license or otherwise acquire and develop additional product candidates or programs.

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

- the public equity market, including pursuant to our at market issuance sales agreement, or the sales agreement, with MLV & Co. LLC, or MLV;
- 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 agreements 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, 2014, we had 61 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 evofosfamide and expect to rely on third parties to manufacture any other product candidates that we may develop. 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 evofosfamide and any other product candidates we may develop could be delayed.

We do not have our own manufacturing capability for the evofosfamide active pharmaceutical ingredient, or API or evofosfamide drug product. Under our license and co-development agreement with Merck KGaA, Merck KGaA has exclusive rights to manufacture evofosfamide for clinical and commercial use, except that we have the right to obtain clinical supply of evofosfamide for clinical trials for United States approval of evofosfamide 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 evofosfamide API and evofosfamide drug product to meet our and Merck KGaA's clinical supply needs of evofosfamide. We have no long-term commitments or commercial supply agreements with any of our evofosfamide 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 evofosfamide 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 evofosfamide, 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 evofosfamide API and drug product manufactured, or if manufacturing is interrupted at our single source contract manufacturers and excipient suppliers for evofosfamide API and evofosfamide 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 evofosfamide clinical program. In any event, we will need to order additional evofosfamide 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 evofosfamide 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 evofosfamide API and drug product. The manufacturing processes improvements for the evofosfamide API may require facilities upgrades at our suppliers, which may lead to delays or disruption in supply, or delays in regulatory approval of evofosfamide. Changes to the formulation of evofosfamide 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 evofosfamide clinical trial material, we may experience a significant delay in our evofosfamide clinical program. Finally, we have not engaged any backup or alternative suppliers for parts of our evofosfamide 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 evofosfamide.

In any event, additional agreements for more supplies of each of our product candidates, including evofosfamide, 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 evofosfamide 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 evofosfamide if approved for commercial sale.

If evofosfamide 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 evofosfamide or increase the manufacturing capacity for evofosfamide or any of our other product candidates in a timely or economically feasible manner. Prior to commercial launch of evofosfamide, 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 evofosfamide 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, adversely impacted by an action of a regulatory agency 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 evofosfamide 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 also expect to rely on contract manufacturers or other third parties to produce sufficient quantities of clinical trial product for any other product candidates that we may develop. In this regard, while we have obtained certain quantities of TH-4000 API and drug product from our licensor, we may determine that such API and drug product is not usable or is otherwise insufficient in order for us to commence or complete our planned Phase 2 proof-of-concept study of TH-4000 and we may need to obtain sufficient supplies of TH-4000 API and drug product from contract manufacturers prior to commencing our planned Phase 2 proof-of-concept study, which could delay the commencement or completion of the planned study, could increase our costs and could negatively impact our planned TH-4000 development program. Depending upon the duration of the clinical studies, we might need to develop a new formulation of TH-4000. It is possible that we might not be able to develop a formulation with adequate quality that meets the need for testing in our clinical trials. In any event, in order for us to commence any planned or potential future clinical trials of our product candidates, we need to obtain or have manufactured sufficient quantities of clinical trial product and there can be no assurance that we will be able to obtain sufficient quantities of clinical trial product in a timely manner or at all. Any delay in receiving sufficient supplies of clinical trial product for our planned or potential future studies could negatively impact our development programs.

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 and foreign agencies for compliance with cGMP regulations, before the respective product candidates can be approved in their region. 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, warning letters, 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 submit NDAs to the FDA, 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 Pharmaceuticals, Inc. to develop and commercialize glufosfamide

We are dependent upon Eleison Pharmaceuticals, Inc., or Eleison 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 evofosfamide and TH-4000, 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 evofosfamide or any other potential future product candidates, then we may not be able to retain or attract collaborators to partner our development programs, including evofosfamide. Further, even if we can obtain protection for and defend the intellectual property position of evofosfamide 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 evofosfamide 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, evofosfamide 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, evofosfamide could potentially compete with doxorubicin or the combination of doxorubicin and ifosfamide, generic products sold by many manufacturers. If approved for commercial sale for treatment-resistant non-small cell lung cancer, TH-4000 could potentially compete with other EGFR-TKIs currently in late-stage clinical development including AstraZeneca's AZD-9291, Clovis Oncology's CO-1686, and Pfizer's dacomitinib. There may also be product candidates of which we are not aware at an earlier stage of development that may compete with evofosfamide, TH-4000 or other product candidates we may develop. In short, each cancer indication for which we are or may be developing product candidates has a number of established medical therapies with which our candidates will compete. Our evofosfamide 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. The laws that may affect our ability to operate include:

- 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. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- 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. Similar to the Federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation;
- 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; and
- 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 and state and foreign laws that 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, patients, healthcare payors and the medical community, we may not generate product revenues sufficient to attain profitability.

If third-party payors do not cover or 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 approved products successfully will depend in part on the extent to which coverage and 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. Coverage and 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 coverage and 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 coverage and 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.

In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, which, among other things, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs and included the following changes to the coverage and payment for drug products under government health care programs:

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extended Medicaid drug rebates, previously due only on fee-for-service utilization, to Medicaid managed care utilization, and created an alternate rebate formula for new formulations of certain existing products that is intended to increase the amount of rebates due on those drugs;
- expanded the types of entities eligible for the 340B drug discount program that mandates discounts to certain hospitals, community centers and other qualifying providers; and
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

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 agencies, 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 evofosfamide;
- 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 evofosfamide 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 regarding our research and development of product candidates, including clinical trial results or delays in the any future clinical trials, or announcements regarding the results of or delays in clinical trials of our product candidates, and investor perceptions thereof;
- 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 us, including under our sales agreement with MLV;
- sales of our common stock by our executive officers, directors and significant 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 options and warrants, which upon such exercise would result in dilution to our security holders.

If we or our existing stockholders sell a large number of shares of our common stock or the public market perceives that we or our existing stockholders might sell shares of our common stock, the market price of our common stock could decline significantly. As of December 31, 2014, we had 62,893,233 outstanding shares of common stock, substantially all of which may be sold in the public market without restriction, subject to any affiliate restrictions. On August 1, 2014, we entered into the Sales Agreement with MLV, under which we may sell shares of our common stock from time to time through MLV, as our agent for the offer and sale of the shares, in an aggregate amount not to exceed $30 million. To the extent that we sell shares of our common stock pursuant to the Sales Agreement with MLV, our stockholders will experience dilution. In addition, a significant number of shares of our common stock are subject to issuance upon the exercise of outstanding options and 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. As of December 31, 2014, warrants to purchase 1,879,062 shares of common stock issued in March 2011 had been exercised. 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 the October 5, 2014 expiration date of the warrants issued in October 2009, all of such warrants had been exercised. On February 18, 2015, we issued warrants to purchase an aggregate of 8,300,000 shares of our common stock, at an initial exercise price per share of $10.86, which exercise price will be subject to adjustment (including to as low as $3.62 per share). In addition, as of December 31, 2014, there were 8,168,942 shares of our common stock issuable upon the exercise of outstanding options having a weighted-average exercise price of $3.69 per share. Although we cannot determine at this time how many of the currently outstanding options and warrants will ultimately be exercised, the options and warrants will likely be exercised only if the exercise price is below the market price of our common stock. To the extent that the options and 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.

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 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, 2014:		
First Quarter	$ 5.93	$ 4.27
Second Quarter	$ 4.88	$ 3.51
Third Quarter	$ 5.41	$ 3.60
Fourth Quarter	$ 3.65	$ 2.58
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

There were approximately 74 holders of record of our common stock as of February 28, 2015.

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, 2014 through December 31, 2014, we issued an aggregate of 2,181,148 shares of our common stock pursuant to the cash exercise of warrants that were originally issued to the investors in our October 2009 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 $2.05 per share, resulting in aggregate cash consideration to us of $4.5 million.

In addition to the cash warrant exercises reported above, from January 1, 2014 through December 31, 2014, we issued an aggregate of 1,108,582 shares of our common stock pursuant to the net, or cashless, exercise of warrants that were originally issued to the investors in our October 2009 private placement. These warrants were exercisable for an aggregate of 2,106,792 shares of common stock and had an exercise price of $2.05 per share. The number of shares issued upon the exercise of these warrants was reduced by an aggregate of 998,210 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.

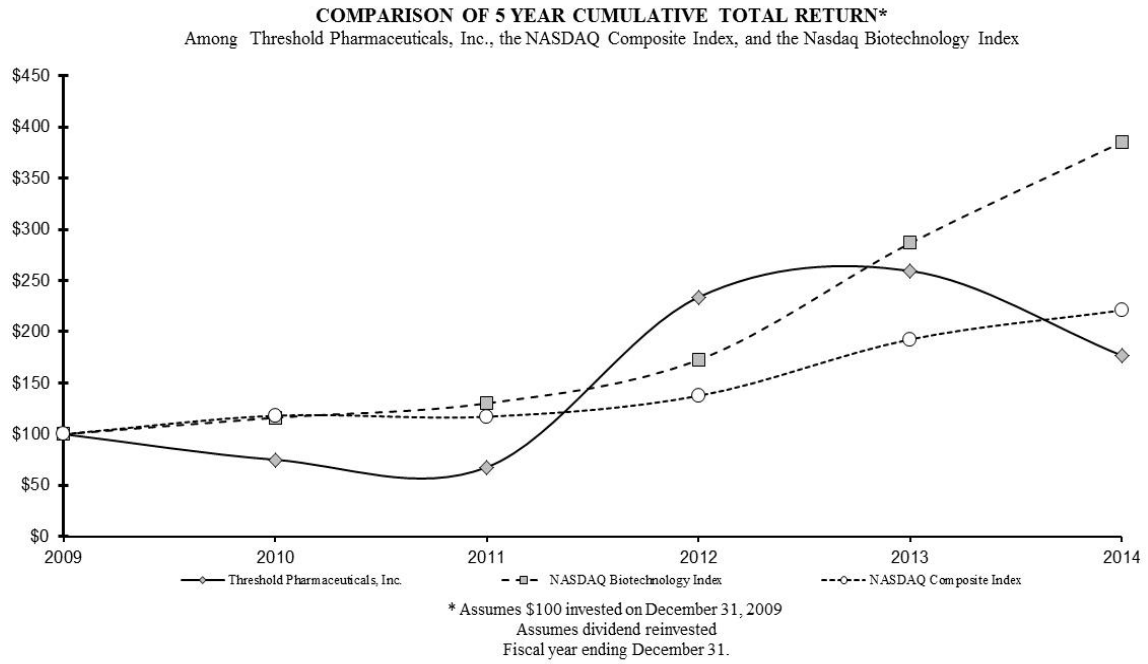
Repurchases of Equity Securities

None.

Stock Performance Graph

The following graph shows the total stockholder return of an investment of $100 in cash on December 31, 2009 for (i) our common stock; (ii) the NASDAQ Composite Index; and (iii) the NASDAQ Biotechnology Index through December 31, 2014. 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,				
	2014	2013	2012	2011	2010
	(In thousands, except per share data)				
Revenue	$ 14,722	$ 12,495	$ 5,867	$ 62	$ —
Operating expenses:					
Research and development (1)	35,832	29,334	18,786	24,388	18,937
General and administrative (1)	10,141	9,185	7,080	5,710	4,971
Total operating expenses	45,973	38,519	25,866	30,098	23,908
Loss from operations	(31,251)	(26,024)	(19,999)	(30,036)	(23,908)
Interest income (expense), net	121	136	80	25	60
Other income (expense), net	9,344	(2,325)	(51,216)	4,358	5,166
Income (loss) before provision for income taxes	(21,786)	(28,213)	(71,135)	(25,653)	(18,682)
Provision (benefit) for income taxes	$ (202)	202	—	—	—
Net loss	$ (21,584)	$ (28,415)	$ (71,135)	$ (25,653)	$ (18,682)
Net loss per common share:					
Basic	$ (0.36)	$ (0.49)	$ (1.31)	$ (0.56)	$ (0.56)
Diluted	$ (0.49)	$ (0.49)	$ (1.31)	$ (0.56)	$ (0.56)
Weighted average number of shares used in net loss per common share calculations:					
Basic	60,335	57,832	54,219	45,900	33,654
Diluted	63,386	57,832	54,219	45,900	33,654
(1) Includes employee and non-employee non-cash stock-based compensation of:					
Research and development	$ 3,123	$ 2,562	$ 1,521	$ 471	$ 381
General and administrative	$ 2,365	$ 2,360	$ 1,489	$ 568	$ 422

	As of December 31,				
	2014	2013	2012	2011	2010
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 58,600	$ 82,033	$ 70,848	$ 20,290	$ 14,699
Working capital	40,706	58,993	70,199	11,953	12,129
Total assets	68,396	104,118	89,521	22,436	16,204
Total liabilities	92,372	127,593	103,374	17,953	11,261
Total stockholders' equity (deficit)	(23,976)	(23,475)	(13,853)	4,483	4,943

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, evofosfamide (formerly TH-302), is being evaluated in two pivotal Phase 3 clinical trials, one registrational Phase 2 clinical trial and multiple earlier-stage clinical trials. We have a global license and co-development agreement for evofosfamide with Merck KGaA, Darmstadt, Germany, with an option to co-commercialize in the United States.

Evofosfamide was discovered by our scientists based on our hypoxia-targeted therapeutics prodrug 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 hematological malignancies (also known as cancers of the bone marrow, for example, leukemias and multiple myeloma). We believe that by virtue of targeting tumor hypoxia, evofosfamide may have broad clinical applicability across many types of solid tumors and some hematological malignancies. To explore this broad therapeutic potential of evofosfamide, we are conducting multiple clinical trials to evaluate its safety and efficacy in solid tumors and hematological malignancies in combination with currently marketed anticancer drugs, including traditional chemotherapeutic agents and antiangiogenic agents, and as monotherapy for certain cancers.

The most advanced clinical study of evofosfamide is a global pivotal Phase 3 clinical trial of evofosfamide plus doxorubicin versus doxorubicin alone in patients with locally advanced unresectable or metastatic soft tissue sarcoma, which we refer to as the 406 trial. The trial enrollment completion was announced in December 2013; the study enrolled 640 patients. In September 2014, we announced that an Independent Data Monitoring Committee, or IDMC, completed the pre-planned interim efficacy and safety analyses of unblinded data for our 406 trial. Based on the IDMC's analyses, which included an assessment of both benefit and risk, the IDMC recommended that the 406 trial should continue as planned to its natural conclusion. We will remain blinded to the data from the 406 trial until the primary efficacy analysis is conducted, which is scheduled to occur after 434 deaths are reported. We currently project that the required number of events will be reached in the latter half of 2015, with the results of the primary efficacy analysis expected to be available shortly thereafter.

In January 2013, we announced that our partner Merck KGaA initiated the global pivotal 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 evofosfamide in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma. The Phase 3 MAESTRO clinical trial was initiated after our randomized and controlled Phase 2 clinical trial of evofosfamide plus gemcitabine versus gemcitabine (which we refer to as the 404 trial) met its primary efficacy endpoint, demonstrating an improvement in progression-free survival when evofosfamide was combined with gemcitabine in this patient population. In October 2014, we announced that our partner Merck KGaA, through its biopharmaceutical division, completed target enrollment of 660 patients in the MAESTRO clinical trial. Currently, we estimate that the protocol-specified events for the MAESTRO trial may be reached in the second half of 2015, with the results of the primary efficacy analysis to be available shortly thereafter. In March 2014, we announced that Merck KGaA initiated a Phase 1 dose escalation study assessing the safety, tolerability and anti-tumor activity of evofosfamide in combination with gemcitabine and nab-paclitaxel (Abraxane®) in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma.

In June 2014, we announced the initiation of a 440-patient, randomized, double-blind, placebo-controlled trial of evofosfamide in combination with pemetrexed in patients with second-line advanced non-squamous non-small cell lung cancer (which we refer to as the 415 trial). The international Phase 2 trial is designed to support registration and will compare the combination of evofosfamide plus pemetrexed versus the combination of pemetrexed plus placebo as second-line therapy in this patient population. The study's primary efficacy endpoint is overall survival and secondary endpoints include safety and assessment of anti-tumor activity as determined by progression-free survival and objective response rate.

In March 2012, we initiated a Phase 1/2 open label clinical trial of evofosfamide to determine the maximum tolerated dose, dose limiting toxicity, safety, tolerability, clinical activity, and pharmacokinetics of evofosfamide in patients with relapsed/refractory multiple myeloma (which we refer to as the 408 trial). Updated results were reported at the June 2014 ASCO annual meeting showing initial signs of clinical activity of the combination of evofosfamide and low dose dexamethasone in patients with extensively treated relapsed/refractory multiple myeloma. In July 2014, we announced the initiation of dosing in the final stage of the 408 trial, which is evaluating evofosfamide in combination with the proteasome inhibitor bortezomib (Velcade®) plus low-dose dexamethasone in patients with relapsed/refractory multiple myeloma. In December 2014, preliminary results from this portion of the trial were reported at December 2014 ASH annual meeting including that the recommended Phase 2 dose of evofosfamide in combination with bortezomib and low-dose dexamethasone was determined to be 340 mg/m^2. Enrollment is ongoing.

Evofosfamide is also the subject of clinical trials investigating evofosfamide as a monotherapy or evofosfamide in combination with antiangiogenic therapies in a variety of tumor types. In August 2013, we announced the initiation of a Phase 2 clinical trial of evofosfamide as single-agent monotherapy in patients with advanced melanoma (which we refer to as the 413 trial). A Phase 1 dose-escalation study of evofosfamide in combination with sunitinib in patients with advanced renal cell carcinoma, or RCC, gastrointestinal stroma tumors, and pancreatic neuroendocrine tumors (which we refer to as the 410 trial) established a recommended phase 2 dose of the combination; additional development opportunities for the investigation of evofosfamide in combination with sunitinib is scheduled to be initiated for the treatment of pancreatic neuroendocrine tumors this year. Two investigator-sponsored trials of evofosfamide are ongoing: a Phase 1/2 study of evofosfamide in combination with bevacizumab in recurrent glioblastoma following bevacizumab failure and a Phase 1/2 study of evofosfamide in combination with sorafenib in advanced RCC and advanced hepatocellular carcinoma. An additional FDA-funded Phase 2 investigator-sponsored trial of evofosfamide in combination with bevacizumab in recurrent glioblastoma following bevacizumab failure is expected to commence in the first half of 2015.

We are working to broaden the potential applicability of evofosfamide as well as to discover additional therapeutics that will selectively target cancer cells. We also seek to optimize patient selectivity for our hypoxia-targeted therapeutics through the development of our [18F]-HX4 investigational hypoxia Positron Emission Tomography (PET) tracer. [18F]-HX4 is a radiolabeled tracer that we acquired from Siemens Healthcare Molecular Imaging to potentially identify and quantify the degree of hypoxia in tumors *in vivo*.

In September 2014, we licensed worldwide rights to a development program from the University of Auckland based on the clinical-stage oncology compound TH-4000 (formerly referred to as PR610, or Hypoxin™), a hypoxia-activated epidermal growth factor receptor, or EGFR, tyrosine-kinase inhibitor (TKI). TH-4000 is designed to selectively release a potent, irreversible EGFR-TKI in hypoxic tumors. Preclinical and Phase 1 clinical data suggest that plasma concentrations of TH-4000 that are active in EGFR-dependent tumor xenograft models in mice could be attained in patients with an acceptable therapeutic index. We expect to initiate a Phase 2 proof-of-concept study in a subset of molecularly-defined non-small cell lung cancer patients who we believe may be responsive to TH-4000 in the first half of 2015.

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, 2014 and December 31, 2013, we had cash, cash equivalents and marketable securities of $58.6 million and $82.0 million, respectively. In February 2015, we completed an underwritten public offering of 8,300,000 shares of our common stock and accompanying warrants to purchase up to 8,300,000 shares of our common stock. We estimate that the net proceeds from the sale of common stock and accompanying warrants, excluding the proceeds, if any, from the exercise of the warrants issued in the offering, will be approximately $28.2 million after deducting the underwriting discount and estimated offering expenses payable by us. For more information on our February 2015 offering, see "Liquidity and Capital Resources" below.

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 evofosfamide development expenses are expected to increase in 2015 compared to 2014 due primarily to the continued execution of existing clinical trials and anticipated commencement of new clinical trials for evofosfamide and TH-4000. 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 evofosfamide are expected to be funded by Merck KGaA, we expect that we will need to raise additional capital to complete the clinical development of evofosfamide, to develop our recently licensed TH-4000 product candidate, 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 $14.7 million and $12.5 million during the years ended December 31, 2014 and 2013, respectively, 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 estimated 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, 2014, 2013 and 2012

Revenue

We recognized $14.7 million and $12.5 million in revenue for the years ended December 31, 2014 and 2013, respectively, 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.

We expect revenue to remain unchanged in 2015 compared to 2014 due to the amortization of milestone payments earned in 2013 and 2012.

Research and Development

Research and development expenses were $35.8 million for the year ended December 31, 2014, compared to $29.3 million for the year ended December 31, 2013 and $18.8 million for the year ended December 31, 2012. The $6.5 million increase in 2014 compared to 2013 was due primarily to a $9.4 million increase in clinical development expenses, a $2.1 million increase in employee-related expenses and a $0.6 million increase in non-cash stock based compensation, partially offset by a $5.6 million increase in reimbursement for Merck KGaA's 70% share of total development expenses for evofosfamide. The $10.5 million increase in 2013 compared to 2012, net of reimbursement for Merck KGaA's 70% share of total development expenses for evofosfamide, was due primarily to a $6.4 million increase in evofosfamide 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.

During the years ended December 31, 2014, 2013 and 2012, we were engaged in two primary research and development programs: the development of evofosfamide, 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. During the year ended December 31, 2014, we were also engaged in preclinical evaluation of our recently-licensed product candidate, TH-4000. 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 evofosfamide) attributable to each of our research and development programs for each period presented:

	Years ended December 31,		
Research and Development Expenses by Project (in thousands):	**2014**	**2013**	**2012**
Evofosfamide	$ 30,094	$ 24,675	$ 14,927
TH-4000	258	—	—
Discovery research	5,480	4,659	3,859
Total research and development expenses	$ 35,832	$ 29,334	$ 18,786

Research and development expenses associated with evofosfamide for 2014 were $30.1 million net of the reimbursement for Merck KGaA's 70% share of total development expenses for evofosfamide compared to $24.7 million net of the reimbursement for Merck KGaA's 70% share of total development expenses for evofosfamide for 2013, and $14.9 million for 2012. The increase of $5.4 million in expenses in 2014 compared to 2013 was due primarily to a $9.3 million increase in clinical development expenses, a $1.4 million increase in employee-related expenses and a $0.4 million in non-cash stock based compensation partially offset by a $5.6 million increase in reimbursement for Merck KGaA's 70% share of total development expenses for evofosfamide and a $0.1 million decrease in consulting expenses. 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 evofosfamide, 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. Evofosfamide 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.

Research and developments expenses associated with TH-4000, which we licensed rights to September 2014, were $0.3 million related to preclinical studies to support further clinical development. Discovery research and development expenses were $5.5 million for 2014, $4.7 million for 2013 and $3.9 million for 2012. We continue to increase our resources and 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, primarily with respect to the clinical development of evofosfamide, and we expect to continue to devote substantial resources to research and development in future periods as we complete our current clinical trials of evofosfamide, start additional clinical trials of evofosfamide and TH-4000, 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 2015 compared to 2014 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 evofosfamide and TH-4000 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 of our research and development programs to be critical to our long-term success. The actual probability of success for evofosfamide, TH-4000 and potential 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 evofosfamide 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, evofosfamide 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. In addition, our development of TH-4000 is at a very early stage and it is possible that TH-4000 may not be found to be safe or effective in our planned Phase 2 proof-of-concept study or in any other studies that we may conduct, and we may otherwise fail to realize the anticipated benefits of our licensing of this product candidate.

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 evofosfamide. 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 $10.1 million for 2014, compared to $9.2 million for 2013 and $7.1 million for 2012. The $0.9 million increase in 2014 compared to 2013 reflects a $0.8 million in higher consulting expenses and $0.1 million in higher staffing and facilities expenses. 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. We currently expect our general and administrative expenses to increase in 2015 compared to 2014 due to increased staffing and consulting expenses to support activities related to our collaboration with Merck KGaA and to the ongoing clinical development of evofosfamide, as well as the planned clinical development of TH-4000.

Interest Income (Expense), Net

Interest income (expense) net for 2014 was $0.1 million of interest income compared to $0.1 million of net interest income for 2013 and $80,000 of net interest income for 2012. 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 2014 was non-cash income of $9.3 million compared to non-cash expense of $2.3 million for 2013 and non-cash expense of $51.2 million for 2012. The non-cash income for 2014 compared to the non-cash expense for 2013 was due to a decrease in the fair value of outstanding warrants to purchase common stock and warrants exercised during 2014 as result of a decrease in the underlying stock price. 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. 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, 2014, we received approximately $4.8 million from the exercise of warrants to purchase approximately 2.3 million shares of common stock. 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 prior at market issuance 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. We had cash, cash equivalents and marketable securities of $58.6 million and $82.0 million at December 31, 2014 and December 31, 2013, respectively, available to fund operations.

In February 2015, we completed an underwritten public offering of 8,300,000 shares of our common stock and accompanying warrants to purchase up to 8,300,000 shares of our common stock. We estimate that the net proceeds from the sale of common stock and accompanying warrants, excluding the proceeds, if any, from the exercise of the warrants issued in the offering, will be approximately $28.2 million after deducting the underwriting discount and estimated offering expenses payable by us.

The warrants issued in the February 2015 offering carry an initial exercise price of $10.86 per share and are exercisable at any time and from time to time commencing with the date six months following the issuance date and continuing through the date that is five years from the issuance date. On the 30th trading day following the earlier of (i) the date two years from the issuance date or (ii) the later to occur of the date on which top-line efficacy data from the 406 trial is publicly announced by us or the date on which top-line efficacy data from the MAESTRO trial is publicly announced by us, the warrant exercise price will be adjusted to equal the average of the volume-weighted average price of our common stock for each of the 20 trading days immediately preceding the applicable date, provided that in no event will the exercise price be adjusted above $10.86 or below $3.62. After the date of foregoing adjustment to the warrant exercise price, which we refer to as the Adjustment Date, the exercise price of the warrants will then be subject to price-based anti-dilution protection such that to the extent we issue and sell any shares of common stock, or any securities convertible or exchangeable for shares of common stock (in each case subject to certain exceptions), at a price per share below the warrant exercise price then in effect, the warrant exercise price will be adjusted downward to the equal the price at which such securities are issued and sold by us (but in no event will the warrant exercise price be reduced below $3.62 per share).

The warrants must be exercised for cash, except that if we fail to maintain an effective registration statement covering the exercise of the warrants, the warrants may be exercised on a net, or cashless basis. In addition, subject to the satisfaction of certain conditions set forth in the warrants, at our option, we have the right to force the holders of the warrants to exercise their warrants in full if the volume-weighted average price of our common stock for any 20 consecutive trading-day period beginning after the 90th day following the Adjustment Date exceeds $18.00 per share.

Net cash used in operating activities for December 31, 2014 was $27.7 million compared to net cash provided by operating activities for the years ended December 31, 2013 and 2012 of $10.2 million and $29.9 million, respectively. The $37.9 million increase in net cash used in operating activities in 2014 compared to 2013 was due to a $30 million decrease in milestone payments from the Merck KGaA collaboration in 2014 compared to 2013. In addition, operating cash payments increased by $7.9 million in 2014 compared to 2013. 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.

Net cash provided by investing activities during the year ended December 31, 2014 was $23.3 million, primarily due to sales and maturities of marketable securities of $68.5 million, partially offset by purchases of investments of $44.9 million. 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 provided by financing activities for the year ended December 31, 2014 was $5.5 million and was primarily due to the approximately $4.8 million proceeds from the exercise of warrants to purchase shares of common stock during 2014. Net cash provided by financing activities for the year ended December 31, 2013 was $2.4 million and was primarily due to the approximately $1.9 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.

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 evofosfamide are expected to be funded by Merck KGaA, we expect that we will need to raise additional capital to complete the clinical development of evofosfamide, to develop our recently licensed TH-4000 product candidate, 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, including pursuant to our at market issuance sales agreement discussed below;
- 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. 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, 2014 are as follows (in thousands):

	Total	Less than one year	One to three years	Four to five years	After five years
Facilities leases	$ 2,109	$ 918	$ 1,191	$ —	$ —
Purchase commitments	3,113	2,758	355	—	—
Total	$ 5,222	$ 3,676	$ 1,546	$ —	$ —

We have not included milestone or royalty payments or other contractual payment obligations in the table above if the amount and timing of such obligations are unknown or uncertain.

At the Market Stock Issuance Facilities

On October 29, 2010, we entered into an at market issuance sales agreement, as amended, or the prior 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 $17.6 million from time to time through MLV as our sales agent. We paid MLV an aggregate commission rate of 3.0% of the gross proceeds of the sales price per share of the common stock sold under the prior sales agreement. 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 prior sales agreement. Net proceeds from the sale of the common stock in 2012 were $12.3 million. In 2013 and 2014, no shares were sold pursuant to the prior sales agreement. In April 2014, the prior sales agreement was terminated.

On August 1, 2014, we entered into a new at market issuance sales agreement, or the current sales agreement, with MLV, which provides that, upon the terms and subject to the conditions and limitations set forth in the current sales agreement, we may elect to issue and sell shares of our common stock having an aggregate offering price of up to $30.0 million from time to time through MLV as our sales agent. Sales of our common stock through MLV, if any, will be made on The NASDAQ Capital Market by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by us and MLV. Subject to the terms and conditions of the current 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 are not obligated to make any sales of common stock under the current sales agreement. We will pay MLV an aggregate commission rate of up to 3.0% of the gross proceeds of the sales price per share of any common stock sold under the current sales agreement. 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. We have not yet sold any common stock pursuant to the current sales agreement. Following the Adjustment Date with respect to the warrants issued in our 2015 public offering, sales of the stock under the current sales agreement could result in a downward adjustment to the exercise price of those warrants.

License and Development Agreements

On September 23, 2014, we entered into an exclusive license agreement with Auckland UniServices Ltd., a wholly-owned company of the University of Auckland. Pursuant to the agreement, we licensed exclusive worldwide rights to a development program based on TH-4000 from the University of Auckland. We expect to initiate a Phase 2 proof-of-concept study in a subset of molecularly-defined non-small cell lung cancer patients who we believe may be responsive to TH-4000 in the first half of 2015. Under the terms of this agreement, we made no upfront payment but we are required to pay all costs of development, as well as annual license maintenance fees starting in 2017, and assuming that we determine to advance the clinical development of TH-4000 beyond our planned Phase 2 proof-of-concept study, we would be required to pay development, regulatory and sales-based milestone payments and royalties on net sales of products, including TH-4000, incorporating technology licensed from the University of Auckland.

On February 3, 2012, we entered into a global license and co-development agreement for evofosfamide 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 evofosfamide in the United States. To date we have received upfront and milestone payments of $110 million. 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 evofosfamide in the soft tissue sarcoma indication. We with Merck KGaA will jointly develop evofosfamide in all other cancer indications being pursued. Merck KGaA will pay 70% of worldwide development costs for evofosfamide. Subject to FDA approval in the United States, Merck KGaA will initially be responsible for commercialization of evofosfamide 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 evofosfamide in the United States. Additionally, we retain the option to co-commercialize evofosfamide 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 evofosfamide 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 evofosfamide in such country or ten years following the commercial launch of a product containing evofosfamide 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, 2014 and 2013, 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, 2014, we recorded an income tax benefit of $0.2 million, which was related to state minimum taxes recorded in the previous year. 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, 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, 2014, we had accumulated approximately $82 million and $87 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, 2014, we had research credit carryforwards of approximately $4.1 million and $4.9 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 2014, 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 evofosfamide. 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.

Recent Accounting Pronouncements Not Yet Adopted

In August 2014, the Financing Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") No. 2014-15,*Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which requires management to evaluate, in connection with preparing financial statements for each annual and interim reporting period, whether there are conditions or events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued and provide related disclosures. This guidance is effective for annual periods ending after December 15, 2016, and, as such, will be applicable to the Company in 2017. Early adoption is permitted. We do not expect this standard to have a material impact on our consolidated financial statements.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue From Contracts With Customers*, requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The updated standard will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective and permits the use of either the retrospective or cumulative effect transition method. Early adoption is not permitted. The updated standard becomes effective for us in the first quarter of fiscal 2017. We have not yet selected a transition method and are currently evaluating the effect that the updated standard will have on our consolidated financial statements and related disclosures.

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

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

We have audited the accompanying consolidated balance sheets of Threshold Pharmaceuticals, Inc. as of December 31, 2014 and 2013, 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, 2014. 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, as well as 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, 2014 and 2013, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, 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, 2014, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 3, 2015, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Jose, California
March 3, 2015

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

	December 31,	
	2014	2013
ASSETS		
Current assets:		
Cash and cash equivalents	$ 8,391	$ 7,279
Marketable securities, current	50,209	58,390
Collaboration receivable	7,248	18,094
Prepaid expenses and other current assets	832	2,246
Total current assets	66,680	86,009
Marketable securities, non-current	—	16,364
Property and equipment, net	557	686
Other assets	1,159	1,059
Total assets	$ 68,396	$ 104,118
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 2,074	$ 1,689
Accrued clinical and development expenses	5,998	7,444
Accrued liabilities	3,180	3,161
Deferred revenue, current	14,722	14,722
Total current liabilities	25,974	27,016
Warrant liability	3,961	23,421
Deferred revenue, non-current	62,194	76,916
Deferred rent	243	240
Total liabilities	92,372	127,593
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, 2014 and 2013; Issued and outstanding: 62,898,233 and 59,232,611 shares at December 31, 2014 and 2013, respectively.	63	59
Additional paid-in capital	349,236	328,116
Accumulated other comprehensive (loss) income	(13)	28
Accumulated deficit	(373,262)	(351,678)
Total stockholders' equity (deficit)	(23,976)	(23,475)
Total liabilities and stockholders' equity (deficit)	$ 68,396	$ 104,118

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,		
	2014	2013	2012
Revenue	$ 14,722	$ 12,495	$ 5,867
Operating expenses:			
Research and development	35,832	29,334	18,786
General and administrative	10,141	9,185	7,080
Total operating expenses	45,973	38,519	25,866
Loss from operations	(31,251)	(26,024)	(19,999)
Interest income (expense), net	121	136	80
Other income (expense), net	9,344	(2,325)	(51,216)
Income (loss) before provision for income taxes	(21,786)	(28,213)	(71,135)
Provision (benefit) for income taxes	(202)	202	—
Net loss	(21,584)	(28,415)	(71,135)
Other comprehensive income (loss):			
Unrealized gain (loss) on available for sale securities	(41)	17	12
Comprehensive loss	$ (21,625)	$ (28,398)	$ (71,123)
Net loss per common share:			
Basic	$ (0.36)	$ (0.49)	$ (1.31)
Diluted	$ (0.49)	$ (0.49)	$ (1.31)
Weighted average number of shares used in per common share calculations:			
Basic	60,335	57,832	54,219
Diluted	63,386	57,832	54,219

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	Accumulated Other Comprehensive	Accumulated	Total Stockholders' Equity
	Shares	Amount	Capital	Income (Loss)	Deficit	(Deficit)
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)
Exercise of warrants to purchase common stock	3,437,348	3	4,831	—	—	4,834
Issuance of common stock pursuant to stock plans	228,274	1	685	—	—	686
Stock-based compensation	—	—	5,488	—	—	5,488
Reclassification of fair value of warrants exercised from liability to equity	—	—	10,116	—	—	10,116
Change in unrealized gain (loss) on marketable securities	—	—	—	(41)	—	(41)
Net loss	—	—	—	—	(21,584)	(21,584)
Balances, December 31, 2014	62,898,233	63	349,236	(13)	(373,262)	(23,976)

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,		
	2014	2013	2012
Cash flows from operating activities:			
Net loss	$ (21,584)	$ (28,415)	$ (71,135)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,309	1,506	1,008
Stock-based compensation expense	5,488	4,922	3,010
Change in common stock warrant value	(9,344)	2,325	51,216
(Gain) loss on sale of investments, property and equipment	(3)	(5)	—
Changes in operating assets and liabilities:			
Collaboration receivable	10,846	(2,459)	(15,635)
Prepaid expenses and other current assets	1,314	(1,079)	(623)
Accounts payable	385	781	(1,481)
Accrued clinical and development expenses	(1,446)	1,694	1,285
Accrued liabilities	19	904	520
Deferred rent	3	(28)	115
Deferred revenue	(14,722)	30,005	61,633
Net cash provided by (used in) operating activities	(27,735)	10,151	29,913
Cash flows from investing activities:			
Acquisition of property and equipment	(224)	(158)	(482)
Acquisition of marketable securities	(44,911)	(101,968)	(93,745)
Proceeds from sales of marketable securities	14,584	5,338	14,266
Proceeds from maturities of marketable securities	53,878	80,495	33,285
Net cash provided by (used in) investing activities	23,327	(16,293)	(46,676)
Cash flows from financing activities:			
Proceeds from issuance of common stock and warrants, net of offering expenses	5,520	2,392	21,910
Net cash provided by financing activities	5,520	2,392	21,910
Net increase (decrease) in cash and cash equivalents	1,112	(3,750)	5,147
Cash and cash equivalents, beginning of period	7,279	11,029	5,882
Cash and cash equivalents, end of period	$ 8,391	$ 7,279	$ 11,029
Non-cash investing and financing activities:			
Change in unrealized gain (loss) in marketable securities	$ (41)	$ 17	$ 12

The accompanying notes are an integral part of these 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, 2014, 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 evofosfamide (formerly 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 the Company's 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. 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 evofosfamide, to develop its recently licensed product candidate, TH-4000 (formerly referred to as PR610 or Hypoxin™), and, 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 agreements 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 its 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 its 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, evofosfamide, has not received any regulatory approvals. To achieve profitable operations, the Company must successfully develop, test, manufacture and market its product candidates, including evofosfamide. With respect to the development and commercialization of evofosfamide, the Company is substantially dependent on Merck KGaA for the continued development and potential commercialization of evofosfamide. In addition, the Company's development of TH-4000 is at a very early stage and it is possible that TH-4000 may not be found to be safe or effective in the Company's planned Phase 2 proof-of-concept study of TH-4000 or in any other studies that the Company may conduct, and the Company may otherwise fail to realize the anticipated benefits of its licensing of this product candidate. There can be no assurance that evofosfamide, TH-4000 or any other of the Company's potential future product candidates will be developed successfully or manufactured at an acceptable cost and with appropriate performance characteristics, or that such products will be successfully marketed. These factors could have a material adverse effect on the Company's future financial results.

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.

Recent Accounting Pronouncements Not Yet Adopted

In August 2014, the Financing Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") No. 2014-15,*Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which requires management to evaluate, in connection with preparing financial statements for each annual and interim reporting period, whether there are conditions or events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued and provide related disclosures. This guidance is effective for annual periods ending after December 15, 2016, and, as such, will be applicable to the Company in 2017. Early adoption is permitted. The Company does not expect this standard to have a material impact on its financial statements.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue From Contracts With Customers*, requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The updated standard will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective and permits the use of either the retrospective or cumulative effect transition method. Early adoption is not permitted. The updated standard becomes effective for the Company in the first quarter of fiscal 2017. The Company has not yet selected a transition method and is currently evaluating the effect that the updated standard will have on its consolidated financial statements and related disclosures.

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 proceeds from the exercise 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,		
	2014	2013	2012
Numerator:			
Net income (loss) - basic	$ (21,584)	$ (28,415)	$ (71,135)
Less: noncash income from change in fair value of common stock warrants	9,344	—	—
Net loss - diluted	(30,928)	$ (28,415)	$ (71,135)
Denominator:			
Weighted-average number of common shares outstanding	60,335	57,832	54,219
Dilutive effect of warrants	3,051	—	—
Weighted-average common shares outstanding and dilutive potential common share-diluted	63,386	57,832	54,219
Net loss per share:			
Basic	$ (0.36)	$ (0.49)	$ (1.31)
Diluted	$ (0.49)	$ (0.49)	$ (1.31)

The following warrants, outstanding options and purchase rights under the Company's 2004 Employee Stock Purchase Plan ("2004 Purchase Plan") 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):

	Years Ended December 31,		
	2014	2013	2012
Shares issuable upon exercise of warrants	—	8,282	11,583
Shares issuable upon exercise of stock options	8,169	6,527	5,099
Shares issuable related to the ESPP	67	64	79

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 evofosfamide, 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 evofosfamide in the United States. To date the Company received $110 million in upfront and milestone payments, including $12.5 million received during the quarter ended March 31, 2014. 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 or was not commensurate with Company's performance subsequent to the inception of the arrangement to achieve the milestone. 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 evofosfamide in the soft tissue sarcoma indication. The Company and Merck KGaA will jointly develop evofosfamide in all other cancer indications being pursued. Merck KGaA will pay 70% of worldwide development expenses for evofosfamide. Subject to FDA approval in the United States, Merck KGaA will initially be responsible for commercialization of evofosfamide 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 evofosfamide in the United States. Additionally, the Company retains the option to co-commercialize evofosfamide 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 evofosfamide 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 evofosfamide in such country or ten years following the commercial launch of a product containing evofosfamide 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 evofosfamide 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 $14.7 million, $12.5 million and $5.9 million of revenue in 2014, 2013 and 2012, respectively. The Company will periodically review and, if necessary, revise the estimated periods of performance of the Company's collaboration. The Company also earned a $21.9 million, $16.5 million and $13.1 million reimbursement for eligible worldwide development expenses for evofosfamide from Merck KGaA in 2014, 2013 and 2012, respectively. Such earned reimbursement has been reflected as a reduction of research and development 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 evofosfamide 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.

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, 2014 and 2013:

	Fair Value as of December 31,	Basis of Fair Value Measurements		
(in thousands)	2014	Level 1	Level 2	Level 3
Money market funds	$ 3,369	$ 3,369	$ —	$ —
Certificates of deposit	2,505	—	2,505	—
Corporate debt securities	28,081	—	28,081	—
Government securities	19,123	—	19,123	—
Commercial paper	5,499	—	5,499	—
Total cash equivalents and marketable securities	$ 58,577	$ 3,369	$ 55,208	$ —

(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	$ —

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, 2014 and 2013:

As of December 31, 2014 (in thousands):	Cost Basis	Unrealized Gain	Unrealized Loss	Fair Value
Money market funds	$ 3,369	$ —	$ —	$ 3,369
Certificates of deposit	2,505	—	—	2,505
Corporate debt securities	28,094	1	(14)	28,081
Government securities	19,123	3	(3)	19,123
Commercial paper	5,499	—	—	5,499
	58,590	4	(17)	58,577
Less cash equivalents	(8,368)	—	—	(8,368)
Total marketable securities	$ 50,222	$ 4	$ (17)	$ 50,209

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

The Company recognized realized gains of $3,000 and $5,000 in 2014 and 2013, respectively. There were no realized losses in 2014 or 2013. There were no realized gains or losses in 2012. The Company realized no gains in 2014 and 2013 that were previously classified as unrealized gains and losses in accumulated other comprehensive income at December 31, 2013 or 2012, respectively.

As of December 31, 2014, weighted average maturity for the Company's available for sale securities was approximately 4 months, with the longest maturity being November 2015.

The following table provides the breakdown of the marketable securities with unrealized losses at December 31, 2014 (in thousands):

As of December 31, 2014 (in thousands):	In loss position for less than twelve months Fair Value	Unrealized Loss
Government securities	$ 11,722	$ 3
Corporate debt securities	18,136	14
Total marketable securities	$ 29,858	$ 17

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 3.8 million shares of outstanding common stock using a Black-Scholes Model. See detailed discussion in Note 8—Stockholders' Equity (Deficit).

NOTE 5—PROPERTY AND EQUIPMENT

Property and equipment comprise the following (in thousands):

	December 31,	
	2014	2013
Computer and office equipment	$ 479	$ 483
Laboratory equipment	1,838	1,703
Leasehold improvements	548	523
	2,865	2,709
Less: Accumulated depreciation and amortization	(2,308)	(2,023)
Total property and equipment, net	$ 557	$ 686

Depreciation and amortization expense was $0.4 million, $0.3 million and $0.2 million for the years ended December 31, 2014, 2013 and 2012, respectively.

NOTE 6—BALANCE SHEET COMPONENTS

Accrued liabilities comprise the following (in thousands):

	December 31,	
	2014	2013
Payroll and employee related expenses	$ 2,808	$ 2,682
Professional services	331	150
Other accrued expenses	41	329
Total accrued liabilities	$ 3,180	$ 3,161

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, 2014, the future rental payments required by the Company for these facilities under noncancelable operating leases are as follows (in thousands):

Years Ending December 31,		
2015	$	918
2016		953
2017		238
Thereafter		—
Total	$	2,109

Rent expense for the years ended December 31, 2014, 2013 and 2012 was $0.8 million, $0.6 million and $0.7 million, respectively.

The Company's purchase commitments at December 31, 2014 were $3.1 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, 2014.

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 (DEFICIT)

Common Stock

On October 29, 2010, the Company entered into an at market issuance sales agreement, as amended, or the prior sales agreement, with MLV & Co., LLC, formerly McNicoll, Lewis & Vlak LLC ("MLV"), pursuant to which the Company was able to issue and sell shares of its common stock having an aggregate offering price of up to $17.6 million from time to time through MLV as sales agent. The Company paid MLV an aggregate commission rate of 3.0% of the gross proceeds of the sales price per share of the common stock sold under the prior sales agreement.During the year ended December 31, 2012, the Company sold 2,022,144 shares of its common stock at an average price of $6.29 pursuant to the prior sales agreement. Net proceeds from the sale of common stock in 2012 were $12.3 million. In 2014 and 2013, there were no shares sold pursuant to the prior sales agreement. In April 2014, the prior sales agreement was terminated.

On August 1, 2014, the Company entered into a new at market issuance sales agreement, or the current sales agreement, with MLV, which provides that, upon the terms and subject to the conditions and limitations set forth in the current sales agreement, the Company may elect to issue and sell shares of its common stock having an aggregate offering price of up to $30.0 million from time to time through MLV as the Company's sales agent. Sales of the Company's common stock through MLV, if any, will be made on The NASDAQ Capital Market by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by the Company and MLV. Subject to the terms and conditions of the current 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 is not obligated to make any sales of common stock under the current sales agreement. The Company will pay MLV an aggregate commission rate of up to 3.0% of the gross proceeds of the sales price per share of any common stock sold under the current sales agreement. The number of shares the Company is able to sell under this arrangement will be limited in practice based on the trading volume of the Company's common stock. The Company has not yet sold any common stock pursuant to the current sales agreement. Under certain circumstances, sales of the stock under the current sales agreement could result in a downward adjustment to the exercise price of the warrants to purchase common stock that the Company issued in February 2015 (see Note 13—Subsequent Events).

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 the Company's 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 had a five-year term and an exercise price equal to $2.23 per share of common stock. The exercise price of the warrants was subject to adjustment 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 was 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 the Company's 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. As of October 5, 2014, 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 2014, warrants to purchase 2,106,792 shares of common stock were cashless exercised for 1,108,582 shares of common stock. In addition, warrants to purchase 2,328,766 shares of common stock were exercised on a cash basis for net proceeds of approximately $4.8 million. 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 on a cash basis 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 on a cash basis 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 $10.1 million and $11.5 million and $27.9 million from warrant liability into stockholders' equity (deficit) in 2014, 2013 and 2012, respectively.

At December 31, 2013, all warrants related to an offering in August 2008 had been exercised. During the years ended December 31, 2013 and 2012, a change in fair value of $2.4 million non-cash expense and $9.9 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, 2014 and 2013, the Company had warrants outstanding to purchase 0 and 4,287,940 shares of common stock, respectively, from the October 2009 offering. All of the warrants related to the October 2009 offering were exercised prior to their expiration date of October 5, 2014. The fair value of these warrants on December 31, 2013 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2014	December 31, 2013
Risk-free interest rate	—	0.13%
Expected life (in years)	—	0.76
Dividend yield	—	—
Volatility	—	49%
Stock price	—	$ 4.67

During the years ended December 31, 2014, 2013 and 2012, a change in fair value of $1.3 million of non-cash income, $0.6 million of non-cash income and $24.2 million of non-cash expense related to the October 2009 warrants was recorded as other income (expense) in the Company's consolidated statements of operations, respectively.

At December 31, 2014 and 2013 the Company had warrants outstanding to purchase 3,846,165 and 3,993,783 shares of common stock, respectively, from the March 2011 offering. The fair value of these warrants on December 31, 2014 and 2013 was determined using a Black Scholes valuation model with the following Level 3 inputs:

	December 31, 2014	December 31, 2013
Risk-free interest rate	0.67%	0.78%
Expected life (in years)	1.21	2.21
Dividend yield	—	—
Volatility	49%	88%
Stock price	$ 3.18	$ 4.67

During the years ended December 31, 2014, 2013 and 2012, a change in the fair value of $8.0 million of non-cash income, $0.5 million of non-cash expense and $17.1 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 October 2009 and March 2011 offerings, subject to fair value measurements as of December 31, 2014 and 2013:

(in thousands)	Fair Value as of December 31, 2014	Basis of Fair Value Measurements Level 1	Level 2	Level 3
March 2011 warrants	$ 3,961	$ —	$ —	$ 3,961

(in thousands)	Fair Value as of December 31, 2013	Basis of Fair Value Measurements 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

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
Exercise of common stock warrants during 2014	(10,116)
Change in fair value of common stock warrants during 2014	(9,344)
Balance at December 31, 2014	$ 3,961

NOTE 9—EQUITY INCENTIVE PLANS AND STOCK BASED COMPENSATION

2004 Equity Incentive Plan

The 2004 Equity Incentive Plan ("2004 Plan") provided for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, stock awards and cash awards to employees and consultants. Stock options were granted under the 2004 Plan with an exercise price not less than 100% of the fair market value of the common stock on the date of grant. Stock options under the 2004 Plan were granted with terms of up to ten years and generally vested over a period of four years. The share reserve under the 2004 Plan was subject to automatic annual increases and on January 1, 2014 an additional 1,250,000 shares of common stock were added to the share reserve under the 2004 Plan. The 2004 Plan expired pursuant to its terms on April 7, 2014. No additional awards have been or will be made after April 7, 2014 under the 2004 Plan.

2014 Equity Incentive Plan

In May 2014, the Company adopted the 2014 Equity Incentive Plan ("2014 Plan"). The terms of the 2014 Plan provide for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, other stock awards, and performance awards that may be settled in cash, stock, or other property. Stock options may be granted under the 2014 Plan with an exercise price not less than 100% of the fair market value of the common stock on the date of grant. Stock options under the 2014 Plan may be granted with terms of up to ten years and generally vest over a period of four years, with the exception of grants to non-employee directors and consultants where the vesting period is or may be shorter. The total number of shares of the Company's common stock initially reserved for issuance under the 2014 Plan was equal to the sum of (i) 6,000,000 newly reserved shares plus (ii) up to 6,626,157 additional shares (the "Prior Plan Shares") that may be added to the 2014 Plan in connection with the forfeiture or expiration of awards outstanding under the 2004 Plan as of May 15, 2014 (the "Returning Shares"). The Prior Plan Shares will be added to the share reserve under the 2014 Plan only as and when such shares become Returning Shares.

Activity under the 2004 and 2014 Plans is set forth below:

	Shares Available for Grant	Outstanding Options		Weighted Average Exercise Price
		Number of Shares	Exercise Price	
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
Additional shares reserved	7,250,000	—		
Shares expired	(1,286,025)	—		
Options granted	(1,895,250)	1,895,250	2.91–4.99	3.78
Options exercised	—	(73,282)	0.64–4.90	1.43
Options canceled	179,532	(179,532)	1.64–6.18	4.63
Balances, December 31, 2014	4,423,493	8,168,942	$ 0.42–7.75	$ 3.69

At December 31, 2014, 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	544,315	3.25	$ 1.11	533,481	$ 1.11
$1.44-$1.44	1,351,681	5.38	$ 1.44	1,351,681	$ 1.44
$1.49-$3.46	1,509,094	6.57	$ 1.98	1,234,515	$ 1.88
$3.62-$3.62	1,449,916	9.36	$ 3.62	265,344	$ 3.62
$4.14-$5.09	1,752,625	8.39	$ 4.97	690,927	$ 5.04
$5.25-$7.75	1,561,311	7.38	$ 6.80	1,095,923	$ 6.75
$0.42-$7.75	8,168,942	7.19	$ 3.69	5,171,871	$ 3.23

The aggregate intrinsic value of options outstanding and options exercisable as of December 31, 2014 were $5.4 million and $5.1 million, respectively. As of December 31, 2014, the ending options vested and expected to vest was 8.1 million and the aggregate intrinsic value of these options was $5.4 million. The weighted average remaining contractual life and weighted average exercise price of these options were 7.18 years and $3.68, 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, 2014.

The total intrinsic value of stock options exercised during the years ended December 31, 2014, 2013 and 2012 were $0.2 million, $0.5 million and $1.7 million, respectively, determined at the date of the option exercise. Cash received from stock option exercises were $0.1 million, $0.1 million and $0.6 million for the years ended December 31, 2014, 2013 and 2012, 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

On January 1, 2014 and 2013 an additional 100,000 shares was authorized for issuance under the 2004 Employee Stock Purchase Plan ("2004 Purchase Plan") pursuant to the annual automatic increase to the authorized shares under the 2004 Purchase Plan. The 2004 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, 2014, employees had purchased 154,992 shares of common stock under the 2004 Purchase Plan at an average price of $3.74. For the year ended December 31, 2013, employees had purchased 167,245 shares of common stock under the 2004 Purchase Plan at an average price of $1.69. At December 31, 2014, 180,904 shares were authorized and available for issuance under the 2004 Purchase Plan.

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):

	Years Ended December 31,		
	2014	2013	2012
Stock-based compensation expense:			
Research and development	$ 3,123	$ 2,562	$ 1,521
General and administrative	2,365	2,360	1,489
	$ 5,488	$ 4,922	$ 3,010

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, 2014, 2013 and 2012:

	Years Ended December 31,		
	2014	2013	2012
Employee Stock Options			
Risk-free interest rate	1.83%	1.14%	1.12%
Expected life (in years)	5.98	5.97	5.99
Dividend yield	—	—	—
Volatility	94%	101%	105%
Weighted-average fair value of stock options granted	$ 2.89	$ 4.04	$ 5.09
Employee Stock Purchase Plan			
Risk-free interest rate	0.20%	0.19%	0.21%
Expected life (in years)	1.24	1.25	1.25
Dividend yield	—	—	—
Volatility	49%	77%	111%
Weighted-average fair value of ESPP purchase rights	$ 1.60	$ 2.27	$ 3.46

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 $5.4 million, $4.8 million and $2.8 million of stock-based compensation expense related to stock options granted and purchase rights granted under the Company's equity compensation plans, for the years ended December 31, 2014, 2013 and 2012, respectively. As of December 31, 2014, the total unrecognized compensation cost related to unvested stock-based awards granted to employees under the Company's equity compensation plans was approximately $10.1 million before estimated forfeitures. This cost will be recorded as compensation expense ratably over the remaining weighted average requisite service period of approximately 2.39 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,		
	2014	2013	2012
Risk-free interest rate	2.52%	2.51%	1.93%
Expected life (in years)	10	10	10
Dividend yield	—	—	—
Expected volatility	97%	100%	101%

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, $0.1 million and $0.2 million for the years ended December 31, 2014, 2013 and 2012, respectively.

NOTE 10—INCOME TAXES

For the year ended December 31, 2014, the Company recorded an income tax benefit of $0.2 million, which was related to state minimum taxes recorded in the prior year. 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, 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):

	2014	2013	2012
U.S. federal taxes (benefit) at statutory rate	$ (7,407)	$ (9,592)	$ (24,186)
State federal income tax benefit	(571)	(1,794)	(1,160)
Unutilized (utilized) net operating losses	9,809	9,747	7,455
Stock-based compensation	730	486	288
Research and development credits	(952)	(1,416)	—
Tax assets not benefited	1,322	1,926	143
Nondeductible warrant expense	(3,177)	790	17,414
Other	44	55	46
Total	$ (202)	$ 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,	
	2014	2013
Capitalized start-up costs	$ 128	$ 179
Net operating loss carryforwards	33,049	31,988
Research and development credits	6,616	5,427
Deferred stock compensation	3,933	3,327
Deferred revenue	26,151	21,151
Other (accruals, reserves, depreciation)	1,019	1,069
Total deferred tax assets	70,896	63,141
Less: Valuation allowance	(70,896)	(63,141)
Net deferred tax assets	$ —	$ —

At December 31, 2014, the Company had federal and state net operating loss carryforwards of approximately $82 million and $87 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, 2014 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, 2014, the Company had federal research and development tax credits of approximately $4.1 million, which expire in the year beginning 2022, and state research and development tax credits of approximately $4.9 million, which have no expiration date.

The Company has established a valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets. The valuation allowance increased by $7.8 million, $11.6 million and by $7.8 million for the years ended December 31, 2014, 2013 and 2012, 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 the Company's gross unrecognized tax benefits:

(in thousands)	2014	2013
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, 2014 and 2013, 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, 2014, 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, 2014. 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.

2014	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share data)				
Revenue	$ 3,681	$ 3,680	$ 3,680	$ 3,681
Net income (loss)	$ (7,109)	$ (766)	$ (7,745)	$ (5,964)
Net income (loss) per common share				
Basic	$ (0.12)	$ (0.01)	$ (0.13)	$ (0.09)
Diluted	$ (0.14)	$ (0.12)	$ (0.15)	$ (0.12)

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)

NOTE 13—SUBSEQUENT EVENTS

Common Stock

On February 18, 2015, the Company completed an underwritten public offering of8.3 million shares of its common stockand accompanying warrants to purchase up to 8.3 million shares of common stock. Net proceeds from the sale of common stock and accompanying warrants, excluding the proceeds, if any, from the exercise of the warrants issued in the offering, are expected to be approximately $28.2 million after deducting the underwriting discount and estimated offering expenses payable by the Company.

The warrants issued in the February 2015 offering carry an initial exercise price of $10.86 per share and are exercisable at any time and from time to time commencing with the date six months following the issuance date and continuing through the date that is five years from the issuance date. On the 30th trading day following the earlier of (i) the date two years from the issuance date or (ii) the later to occur of (a) the date on which top-line efficacy data from the Company's Phase 3 clinical trial of evofosfamide plus doxorubicin versus doxorubicin alone in patients with locally advanced unresectable or metastatic soft tissue sarcoma is publicly announced by the Company or (b) the date on which top-line efficacy data from the Phase 3 MAESTRO clinical trial of evofosfamide in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma is publicly announced by the Company, the warrant exercise price will be adjusted to equal the average of the volume-weighted average price of the Company's common stock for each of the 20 trading days immediately preceding the applicable date, provided that in no event will the exercise price be adjusted above $10.86 or below $3.62. After the date of foregoing adjustment to the warrant exercise price (such date, the "Adjustment Date"), the exercise price of the warrants will then be subject to price-based anti-dilution protection such that to the extent the Company's issues and sells any shares of common stock, or any securities convertible or exchangeable for shares of common stock (in each case subject to certain exceptions), at a price per share below the warrant exercise price then in effect, the warrant exercise price will be adjusted downward to the equal the price at which such securities are issued and sold by the Company (but in no event will the warrant exercise price be reduced below $3.62 per share).

The exercise price of the warrants are also be subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the Company's common stock. The warrants must be exercised for cash, except that if the Company fails to maintain an effective registration statement covering the exercise of the warrants, the warrants may be exercised on a net, or cashless basis. In addition, subject to the satisfaction of certain conditions set forth in the warrants, at the Company's option, the Company has the right to force the holders of the warrants to exercise their warrants in full if the volume-weighted average price of the Company's common stock for any 20 consecutive trading-day period beginning after the 90th day following the Adjustment Date exceeds $18.00 per share.

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, 2014, 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* (2013 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, 2014.

Our independent registered public accounting firm, Ernst & Young LLP, has audited our internal control over financial reporting as of December 31, 2014. 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, 2014 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, 2014, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 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, 2014, 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, 2014 and 2013, 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, 2014 of Threshold Pharmaceuticals, Inc. and our report dated March 3, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Jose, California
March 3, 2015

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 2014 fiscal year pursuant to Regulation 14A for our 2014 Annual Meeting of Stockholders, or the 2015 Proxy Statement, and the information to be included in the 2015 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 2015 Proxy Statement and is hereby incorporated by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be contained in the 2015 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 2015 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 2015 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 2015 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 3, 2015

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 3, 2015
/s/ JOEL A. FERNANDES **Joel A. Fernandes**	Vice President, Finance and Controller (principal financial and accounting officer)	March 3, 2015
/s/ JEFFREY W. BIRD, M.D., PH.D. **Jeffrey W. Bird, M.D., Ph.D.**	Director	March 3, 2015
/s/ BRUCE C. COZADD **Bruce C. Cozadd**	Director	March 3, 2015
/s/ DAVID R. HOFFMANN **David R. Hoffmann**	Director	March 3, 2015
/s/ WILFRED E. JAEGER, M.D. **Wilfred E. Jaeger, M.D.**	Director	March 3, 2015
/s/ GEORGE G. C. PARKER, PH.D. **George G. C. Parker, Ph.D.**	Director	March 3, 2015
/s/ DAVID R. PARKINSON, M.D. **David R. Parkinson, M.D.**	Director	March 3, 2015

EXHIBIT INDEX

EXHIBIT NUMBER	DESCRIPTION
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as subsequently amended (incorporated by reference to Exhibit 3.1 to the Registrant's Annual Report on Form 10-K (File No. 001-32979) filed on March 6, 2014)
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 (File No. 000-51136) 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 (File No. 000-51136) 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 (File No. 001-32979) 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 (File No. 001-32979) 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 (File No. 001-32979) filed on March 11, 2011)
4.7	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 (File No. 001-32979) filed on March 11, 2011)
4.9*	Form of Warrant issued pursuant to the Registrant's prospectus supplement, dated February 11, 2015, and accompanying prospectus.
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 (File No. 001-32979) 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 under the 2004 Equity Incentive Plan (incorporated by reference to Exhibit 10.25 (File No. 000-51136) to the Registrant's Current Report on Form 8-K filed on March 17, 2006)
10.5+	2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-32979) filed on May 21, 2014).
10.6+	Form of Stock Option Grant Notice and Option Agreement for employees under the 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-32979) filed on May 21, 2014).
10.7+	Form of Stock Option Grant Notice and Option Agreement for non-employee directors under the 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-32979) filed on May 21, 2014).

10.8+	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 (File No. 001-32979) filed on November 2, 2007)
10.9	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 (File No. 001-32979) filed on July 14, 2008)
10.10	Form of Securities Purchase Agreement dated as of September 29, 2009 (incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K (File No. 001-32979) filed on September 30, 2009)
10.11+	Form of Amended and Restated Change of Control Severance Agreement for employees at the Senior Vice President level and above (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-32979) filed on April 12, 2012)
10.12+	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 (File No. 001-32979) filed on April 12, 2012)
10.13+	Change of Control Severance Agreement by and between the Registrant and Stewart M. Kroll dated April 9, 2012 (incorporated by reference to Exhibit 10.3 to our Current Report on Form 8-K (File No. 001-32979) filed on April 12, 2012)
10.14+*	Form of Change of Control Severance Agreement for employees at the Vice President level
10.15†	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 (File No. 001-32979) filed on March 8, 2010)
10.16†	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 (File No. 001-32979), filed on August 6, 2012)
10.17†	Amendment to License and Co-Development Agreement between the Registrant and Merck KGaA, dated December 2, 2013 (incorporated by reference to Exhibit 10.11 to the Registrant's Annual Report on Form 10-K (File No. 001-32979) filed on March 6, 2014)
10.18	At Market Issuance Sales Agreement, dated August 1, 2014, by and between Threshold Pharmaceuticals, Inc. and MLV & Co., LLC. (incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-32979), filed on August 1, 2014)
10.19	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 (File No. 001-32979), filed on November 3, 2011)
10.20+	Advisory Board Agreement by and between the Registrant and David R. Parkinson, M.D. (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-32979), filed on May 1, 2014)
10.21+	Non-Employee Director Compensation Policy, adopted by the Board of Directors of the Registrant on March 20, 2014 (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-32979), filed on May 1, 2014)
12.1*	Statement of Computation of Ratio of Earnings to Fixed Charges and Ratio of Earnings to Combined Fixed Charges and Preferred Stock Dividends
23.1*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
24.1*	Power of Attorney (included on the signature page hereto).
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
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

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* Filed herewith.

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

+ Indicates a management contract or compensatory plan or arrangement.

** 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.

PURSUANT TO THE TERMS OF SECTION 1 AND SECTION 15 OF THIS WARRANT, ALL OR A PORTION OF THIS WARRANT MAY HAVE BEEN EXERCISED OR CANCELED, AND THEREFORE THE ACTUAL NUMBER OF WARRANT SHARES REPRESENTED BY THIS WARRANT MAY BE LESS THAN THE AMOUNTS SET FORTH ON THE FACE HEREOF. ANY TRANSFEREE OF THIS WARRANT SHOULD CONTACT THRESHOLD PHARMACEUTICALS, INC. IN ADVANCE OF ACQUIRING THIS WARRANT TO BE APPRISED OF THE ACTUAL NUMBER OF SHARES THAT MAY BE ACQUIRED PURSUANT TO THE EXERCISE OF THIS WARRANT.

THRESHOLD PHARMACEUTICALS, INC.

FORM OF

WARRANT TO PURCHASE COMMON STOCK

Warrant No.:
Number of Shares of Common Stock:_____
Date of Issuance: February 18, 2015 ("**Issuance Date**")

Threshold Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), hereby certifies that, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, [_____], the registered holder hereof or its permitted assigns (the "**Holder**"), is entitled, subject to the terms set forth below, to purchase from the Company, at the Exercise Price (as defined below) then in effect, upon exercise of this Warrant to Purchase Common Stock (including any Warrants to Purchase Common Stock issued in exchange, transfer or replacement hereof, the "**Warrant** "), at any time or times on or after the date that is six-months following the Issuance Date (the "**Exercisability Date**"**)**, but not after 11:59 p.m., New York time, on the Expiration Date (as defined below), _____ (_____) fully paid nonassessable shares of Common Stock (as defined below) (the "**Warrant Shares**"). Except as otherwise defined herein, capitalized terms in this Warrant shall have the meanings set forth in Section 16.

This Warrant is one of a series of warrants to purchase Common Stock issued pursuant to that certain underwriting agreement, dated as of February 11, 2015 (the "**Agreement**"), by and between the Company and Jefferies LLC, as representative of the several underwriters listed on Schedule A thereto (all such warrants, excluding this Warrant, collectively, the "**Other Warrants**"), pursuant to the Company's Registration Statement on Form S-3 (File number 333-195084) (the "**Registration Statement**").

1. EXERCISE OF WARRANT.

(a) Mechanics of Exercise. Subject to the terms and conditions hereof, this Warrant may be exercised by the Holder on any day on or after the Exercisability Date, in whole or in part, by delivery of a written notice, in the form attached hereto as Exhibit A (the "**Exercise Notice**"), of the Holder's election to exercise this Warrant. Within one (1) day

following the Exercise Notice (the "**Payment Deadline**") (if a registration statement registering the issuance of the Warrant Shares under the Securities Act of 1933, as amended (the "**Securities Act**"), is effective and available for the issuance of the Warrant Shares)**,** the Holder shall make payment to the Company of an amount equal to the applicable Exercise Price multiplied by the number of Warrant Shares as to which this Warrant is being exercised (the "**Aggregate Exercise Price**") in cash or by wire transfer of immediately available funds, or provided the conditions for cashless exercise set forth in Section 1(d) are satisfied, by notifying the Company that this Warrant is being exercised pursuant to a Cashless Exercise (as defined in Section 1(d)). The Holder shall not be required to deliver the original Warrant in order to effect an exercise hereunder; provided, however, that in the event that this Warrant is exercised in full or for the remaining unexercised portion hereof, the Holder shall deliver this Warrant to the Company for cancellation within a reasonable time after such exercise. Execution and delivery of the Exercise Notice with respect to less than all of the Warrant Shares shall have the same effect as cancellation of the original Warrant and issuance of a new Warrant evidencing the right to purchase the remaining number of Warrant Shares**;** provided that Holder shall have complied with its obligation to deliver the Aggregate Exercise Price no later than the Payment Deadline. On or before the first (1st) Business Day following the date on which the Company has received the Exercise Notice, the Company shall transmit by facsimile or e-mail transmission an acknowledgment of confirmation of receipt of the Exercise Notice to the Holder and the Company's transfer agent for the Common Stock (the "**Transfer Agent**"). Provided that Holder shall have complied with its obligation to deliver the Aggregate Exercise Price no later than the Payment Deadline, on or before the third (3rd) Trading Day following the date on which the Company has received the Exercise Notice (the "**Share Delivery Date**"), the Company shall (X) provided that the Transfer Agent is participating in The Depository Trust Company ("**DTC**") Fast Automated Securities Transfer Program, upon the request of the Holder, credit such aggregate number of Warrant Shares to which the Holder is entitled pursuant to such exercise to the Holder's or its designee's balance account with DTC through its Deposit Withdrawal Agent Commission system, or (Y) if the Transfer Agent is not participating in the DTC Fast Automated Securities Transfer Program, issue and dispatch by overnight courier to the address as specified in the Exercise Notice, a certificate, registered in the Company's share register in the name of the Holder or its designee, for the number of shares of Common Stock to which the Holder is entitled pursuant to such exercise. Upon delivery of the Exercise Notice and provided that Holder shall have complied with its obligation to deliver the Aggregate Exercise Price no later than the Payment Deadline, the Holder shall be deemed for all corporate purposes to have become the holder of record of the Warrant Shares with respect to which this Warrant has been exercised, irrespective of the date such Warrant Shares are credited to the Holder's DTC account or the date of delivery of the certificates evidencing such Warrant Shares, as the case may be. If this Warrant is submitted in connection with any exercise pursuant to this Section 1(a) and the number of Warrant Shares represented by this Warrant submitted for exercise is greater than the number of Warrant Shares being acquired upon an exercise, then the Company shall as soon as practicable and in no event later than three Trading Days after any exercise and at its own expense, issue a new Warrant (in accordance with Section 7(e)) representing the right to purchase the number of Warrant Shares purchasable immediately prior to such exercise under this Warrant, less the number of Warrant Shares with respect to which this Warrant is exercised. No fractional shares of Common Stock are to be issued upon the exercise of this Warrant, but rather the number of shares of Common Stock to be issued shall be rounded up to the nearest

whole number. The Company shall pay any and all taxes which may be payable with respect to the issuance and delivery of Warrant Shares upon exercise of this Warrant; provided, however , that the Company shall not be required to pay any tax which may be payable in respect of any transfer involved in the registration of any certificates for Warrant Shares or Warrant(s) in a name other than that of the Holder or an affiliate thereof. The Holder shall be responsible for all other tax liability that may arise as a result of holding or transferring this Warrant or receiving Warrant Shares upon exercise hereof.

(b) Exercise Price. For purposes of this Warrant, "**Exercise Price**" initially means $10.86, subject to adjustment as provided herein. On the thirtieth (30th) Trading Day following the Data Release Date (the "**Adjustment Date**"), the Exercise Price shall be changed to equal the Market Price on the Adjustment Date; provided, however, that in no event shall the Exercise Price, including for purposes of this Section 1(b) and for all other purposes of this Warrant, exceed $10.86 (the "**Ceiling Price**") or be less than $3.62 (the "**Floor Price**"), in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock occurring after the Issuance Date.

(c) Company's Failure to Timely Deliver Securities. If the Company shall fail for any reason or for no reason to issue to the Holder within three (3) Business Days of receipt of the Exercise Notice in compliance with the terms of this Section 1, a certificate for the number of Warrant Shares to which the Holder is entitled and register such shares of Common Stock on the Company's share register or to credit the Holder's balance account with DTC for such number of Warrant Shares of Common Stock to which the Holder is entitled upon the Holder's exercise of this Warrant, and if on or after such Trading Day the Holder purchases (in an open market transaction or otherwise) shares of Common Stock to deliver in satisfaction of a sale by the Holder of shares of Common Stock issuable upon such exercise that the Holder anticipated receiving from the Company (a "**Buy-In**"), then the Company shall, within three (3) Business Days after the Holder's request and in the Holder's discretion, either (i) pay cash to the Holder in an amount equal to the Holder's total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased (the "**Buy-In Price**"), at which point the Company's obligation to deliver such certificate (and to issue such Warrant Shares or credit such Holder's balance account with DTC) shall terminate, or (ii) promptly honor its obligation to deliver to the Holder a certificate or certificates representing such Warrant Shares or credit such Holder's balance account with DTC and pay cash to the Holder in an amount equal to the excess (if any) of the Buy-In Price over the product of (A) such number of shares of Common Stock, times (B) the Closing Bid Price on the date of exercise.

(d) Cashless Exercise. Notwithstanding anything contained herein to the contrary, if a registration statement registering the issuance of the Warrant Shares under the Securities Act is not effective or available for the issuance of the Warrant Shares, then the Holder may only exercise this Warrant, whether whole or in part, and in lieu of making the cash payment otherwise contemplated to be made to the Company upon such exercise in payment of the Aggregate Exercise Price, by receiving upon such exercise the "Net Number" of shares of Common Stock determined according to the following formula (a "**Cashless Exercise**"):

Net Number = (A x B) - (A x C)
B

For purposes of the foregoing formula:

A= the total number of shares with respect to which this Warrant is then being exercised.

B= the arithmetic average of Closing Sale Prices of the shares of Common Stock for the five (5) consecutive Trading Days ending on the date immediately preceding the date of the Exercise Notice.

C= the Exercise Price then in effect for the applicable Warrant Shares at the time of such exercise.

(e) Rule 144 . For purposes of Rule 144(d) promulgated under the Securities Act, as in effect on the date hereof, it is intended that the Warrant Shares issued in a Cashless Exercise shall be deemed to have been acquired by the Holder, and the holding period for the Warrant Shares shall be deemed to have commenced, on the date this Warrant was originally issued.

(f) Disputes. In the case of a dispute as to the determination of the Exercise Price or the arithmetic calculation of the Warrant Shares, the Company shall promptly issue to the Holder the number of Warrant Shares that are not disputed.

(g) Beneficial Ownership Limitation. The Company shall not effect the exercise of this Warrant, and the Holder shall not have the right to exercise this Warrant, to the extent that after giving effect to such exercise, such Holder (together with such Holder's affiliates and any other Persons whose beneficial ownership of shares of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended (the "**1934 Act**")) would beneficially own in excess of 4.99% (the "**Maximum Percentage**") of the shares of Common Stock outstanding immediately after giving effect to such exercise. For purposes of the foregoing sentence, the aggregate number of shares of Common Stock beneficially owned by such Holder, its affiliates and any other Persons whose beneficial ownership of shares of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) of the 1934 Act shall include the number of shares of Common Stock issuable upon exercise of this Warrant with respect to which the determination of such sentence is being made, but shall exclude shares of Common Stock which would be issuable upon (i) exercise of the remaining, unexercised portion of this Warrant beneficially owned by such Holder and its affiliates and any other Persons whose beneficial ownership of shares of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) of the 1934 Act, and (ii) exercise or conversion of the unexercised or unconverted portion of any other securities of the Company beneficially owned by such Holder and its affiliates and any other Persons whose beneficial ownership of shares of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) of the 1934 Act (including, without limitation, any convertible notes or convertible preferred stock or warrants) subject to a limitation on conversion or exercise analogous to the limitation contained herein. Except as set forth in the preceding sentence, for purposes of this paragraph, beneficial ownership shall be calculated in accordance with

Section 13(d) of the 1934 Act. For purposes of this Warrant, in determining the number of outstanding shares of Common Stock, the Holder may rely on the number of outstanding shares of Common Stock as reflected in (1) the Company's most recent Form 10-K, Form 10-Q, Current Report on Form 8-K or other public filing with the Securities and Exchange Commission, as the case may be, (2) a more recent public announcement by the Company or (3) any other notice by the Company or the Transfer Agent setting forth the number of shares of Common Stock outstanding. For any reason at any time, upon the written or oral request of the Holder, the Company shall within one (1) Business Day confirm orally and in writing to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including the Warrants, by the Holder and its affiliates since the date as of which such number of outstanding shares of Common Stock was reported. By written notice to the Company, the Holder may from time to time increase or decrease the Maximum Percentage to any other percentage not in excess of 9.99% or less than 4.99% specified in such notice; provided that (i) any such increase will not be effective until the sixty-first (61st) day after such notice is delivered to the Company, and (ii) any such increase or decrease will apply only to the Holder and not to any other holder of the Warrants. For the avoidance of doubt, to the extent the limitation set forth in this Section 1(g) applies, the determination (i) of whether the exercise of this Warrant may be effected (vis-a-vis other Options or Convertible Securities owned by the Holder or any of its affiliates and any other Persons whose beneficial ownership of shares of Common Stock would be aggregated with the Holder's for purposes of Section 13(d) of the 1934 Act) and (ii) of which such Options or Convertible Securities shall be convertible, exercisable or exchangeable (as the case may be, as among all such securities owned by the Holder) shall, subject to such Maximum Percentage limitation, be determined on the basis of the first submission to the Company for conversion, exercise or exchange (as the case may be). The provisions of this paragraph shall be construed and implemented in a manner other than in strict conformity with the terms of this Section 1(g) to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended beneficial ownership limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation.

2. ADJUSTMENT OF EXERCISE PRICE AND NUMBER OF WARRANT SHARES. The Exercise Price and the number of Warrant Shares shall be adjusted from time to time as follows:

Stock Dividends and Splits

. Without limiting any provision of Section 2(b) or Section 4, if the Company, at any time on or after the Issuance Date, (i) pays a stock dividend on one or more classes of its then outstanding shares of Common Stock or otherwise makes a distribution on any class of capital stock that is payable in shares of Common Stock, (ii) subdivides (by any stock split, stock dividend, recapitalization or otherwise) one or more classes of its then outstanding shares of Common Stock into a larger number of shares or (iii) combines (by combination, reverse stock split or otherwise) one or more classes of its then outstanding shares of Common Stock into a smaller number of shares, then in each such case the Exercise Price shall be multiplied by a fraction of which the numerator shall be the number of shares of Common Stock outstanding immediately before such event and of which the denominator shall be the number of shares of Common Stock outstanding immediately after such event. Any adjustment made pursuant to clause (i) of this paragraph shall become effective immediately

after the record date for the determination of stockholders entitled to receive such dividend or distribution, and any adjustment pursuant to clause (ii) or (iii) of this paragraph shall become effective immediately after the effective date of such subdivision or combination. If any event requiring an adjustment under this paragraph occurs during the period that the Exercise Price is calculated hereunder, then the calculation of such Exercise Price shall be adjusted appropriately to reflect such event.

(b) Adjustment Upon Issuance of Shares of Common Stock. If and whenever on or after the Adjustment Date, the Company issues or sells, or in accordance with this Section 2(b) is deemed to have issued or sold, any shares of Common Stock (including the issuance or sale of shares of Common Stock owned or held by or for the account of the Company, but excluding any Excluded Securities issued or sold or deemed to have been issued or sold) for a consideration per share (the "**New Issuance Price**") less than a price equal to the Exercise Price in effect immediately prior to such issue or sale or deemed issuance or sale (such Exercise Price then in effect is referred to as the "**Applicable Price**") (the foregoing a "**Dilutive Issuance**"), then immediately after such Dilutive Issuance, the Exercise Price then in effect shall be reduced to an amount equal to the New Issuance Price. For purposes of determining the adjusted Exercise Price under this Section 2(b), the following shall be applicable:

(i) Issuance of Options. If the Company in any manner grants or sells any Options and the lowest price per share for which one share of Common Stock is issuable upon the exercise of any such Option or upon conversion, exercise or exchange of any Convertible Securities issuable upon exercise of any such Option is less than the Applicable Price, then such share of Common Stock shall be deemed to be outstanding and to have been issued and sold by the Company at the time of the granting or sale of such Option for such price per share. For purposes of this Section 2(b)(i), the "lowest price per share for which one share of Common Stock is issuable upon the exercise of any such Options or upon conversion, exercise or exchange of any Convertible Securities issuable upon exercise of any such Option" shall be equal to (1) the lower of (x) the sum of the lowest amounts of consideration (if any) received or receivable by the Company with respect to any one share of Common Stock upon the granting or sale of such Option, upon exercise of such Option and upon conversion, exercise or exchange of any Convertible Security issuable upon exercise of such Option and (y) the lowest exercise price set forth in such Option for which one share of Common Stock is issuable upon the exercise of any such Options or upon conversion, exercise or exchange of any Convertible Securities issuable upon exercise of any such Option minus (2) the sum of all amounts paid or payable to the holder of such Option (or any other Person) upon the granting or sale of such Option, upon exercise of such Option and upon conversion, exercise or exchange of any Convertible Security issuable upon exercise of such Option plus the value of any other consideration received or receivable by, or benefit conferred on, the holder of such Option (or any other Person). Except as contemplated below, no further adjustment of the Exercise Price shall be made upon the actual issuance of such shares of Common Stock or of such Convertible Securities upon the exercise of such Options or upon the actual issuance of such shares of Common Stock upon conversion, exercise or exchange of such Convertible Securities.

(ii) Issuance of Convertible Securities. If the Company in any manner issues or sells any Convertible Securities and the lowest price per share for which one share of Common Stock is issuable upon the conversion, exercise or exchange thereof is less

than the Applicable Price, then such share of Common Stock shall be deemed to be outstanding and to have been issued and sold by the Company at the time of the issuance or sale of such Convertible Securities for such price per share. For the purposes of this Section 2(b)(ii), the "lowest price per share for which one share of Common Stock is issuable upon the conversion, exercise or exchange thereof" shall be equal to (1) the lower of (x) the sum of the lowest amounts of consideration (if any) received or receivable by the Company with respect to one share of Common Stock upon the issuance or sale of the Convertible Security and upon conversion, exercise or exchange of such Convertible Security and (y) the lowest conversion price set forth in such Convertible Security for which one share of Common Stock is issuable upon conversion, exercise or exchange thereof minus (2) the sum of all amounts paid or payable to the holder of such Convertible Security (or any other Person) upon the issuance or sale of such Convertible Security plus the value of any other consideration received or receivable by, or benefit conferred on, the holder of such Convertible Security (or any other Person). Except as contemplated below, no further adjustment of the Exercise Price shall be made upon the actual issuance of such shares of Common Stock upon conversion, exercise or exchange of such Convertible Securities, and if any such issue or sale of such Convertible Securities is made upon exercise of any Options for which adjustment of this Warrant has been or is to be made pursuant to other provisions of this Section 2(b), except as contemplated below, no further adjustment of the Exercise Price shall be made by reason of such issue or sale.

(iii) Change in Option Price or Rate of Conversion. If the purchase or exercise price provided for in any Options, the additional consideration, if any, payable upon the issue, conversion, exercise or exchange of any Convertible Securities, or the rate at which any Convertible Securities are convertible into or exercisable or exchangeable for shares of Common Stock increases or decreases at any time, the Exercise Price in effect at the time of such increase or decrease shall be adjusted to the Exercise Price which would have been in effect at such time had such Options or Convertible Securities provided for such increased or decreased purchase price, additional consideration or increased or decreased conversion rate, as the case may be, at the time initially granted, issued or sold. For purposes of this Section 2(b)(iii), if the terms of any Option or Convertible Security that was outstanding as of the date of issuance of this Warrant are increased or decreased in the manner described in the immediately preceding sentence, then such Option or Convertible Security and the shares of Common Stock deemed issuable upon exercise, conversion or exchange thereof shall be deemed to have been issued as of the date of such increase or decrease. No adjustment pursuant to this Section 2(b) shall be made if such adjustment would result in an increase of the Exercise Price then in effect.

(iv) Calculation of Consideration Received. If any Option or Convertible Security or Adjustment Right is issued in connection with the issuance or sale or deemed issuance or sale of any other securities of the Company, together comprising one integrated transaction, (x) such Option or Convertible Security (as applicable) or Adjustment Right (as applicable) will be deemed to have been issued for consideration equal to the Option Value thereof and (y) the other securities issued or sold or deemed to have been issued or sold in such integrated transaction shall be deemed to have been issued for consideration equal to the difference of (I) the aggregate consideration received or receivable by the Company minus (II) the Option Value of each such Option or Convertible Security (as applicable) or Adjustment Right (as applicable). If any shares of Common Stock, Options or Convertible Securities are issued or sold or deemed to have been issued or sold for cash, the consideration received therefor

will be deemed to be the net amount of consideration received by the Company therefor. If any shares of Common Stock, Options or Convertible Securities are issued or sold for a consideration other than cash, for purposes of calculating the consideration paid for the Options or Convertible Securities (but not the Option Value thereof), the amount of such consideration received by the Company will be the fair value of such consideration, except where such consideration consists of publicly traded securities, in which case the amount of consideration received by the Company for such securities will be the arithmetic average of the VWAPs of such security for each of the five (5) Trading Days immediately preceding the date of receipt. If any shares of Common Stock, Options or Convertible Securities are issued to the owners of the non-surviving entity in connection with any merger in which the Company is the surviving entity, the amount of consideration therefor will be deemed to be the fair value of such portion of the net assets and business of the non-surviving entity as is attributable to such shares of Common Stock, Options or Convertible Securities, as the case may be. The fair value of any consideration other than cash or publicly traded securities (but not the Option Value thereof) will be determined jointly by the Company and the Holder. If such parties are unable to reach agreement within ten (10) days after the occurrence of an event requiring valuation (the "**Valuation Event**"), the fair value of such consideration will be determined within five (5) Trading Days after the tenth (10th) day following such Valuation Event by an independent, reputable appraiser jointly selected by the Company and the Holder. The determination of such appraiser shall be final and binding upon all parties absent manifest error and the fees and expenses of such appraiser shall be borne by the Company.

(v) Record Date. If the Company takes a record of the holders of shares of Common Stock for the purpose of entitling them (A) to receive a dividend or other distribution payable in shares of Common Stock, Options or in Convertible Securities or (B) to subscribe for or purchase shares of Common Stock, Options or Convertible Securities, then such record date will be deemed to be the date of the issue or sale of the shares of Common Stock deemed to have been issued or sold upon the declaration of such dividend or the making of such other distribution or the date of the granting of such right of subscription or purchase (as the case may be).

Number of Warrant Shares

. Simultaneously with any adjustment to the Exercise Price pursuant to Section 2(a), the number of Warrant Shares that may be purchased upon exercise of this Warrant shall be increased or decreased proportionately, so that after such adjustment the aggregate Exercise Price payable hereunder for the adjusted number of Warrant Shares shall be the same as the aggregate Exercise Price in effect immediately prior to such adjustment (without regard to any limitations on exercise contained herein).

Other Events

. If any event occurs of the type contemplated by the provisions of this Section 2 but not expressly provided for by such provisions (including, without limitation, the granting of stock appreciation rights, phantom stock rights or other rights with equity features), then the Company's board of directors shall in good faith determine and implement an appropriate adjustment in the Exercise Price and/or the number of Warrant Shares (if applicable) so as to protect the rights of the Holder, provided that no such adjustment pursuant to this Section 2(d) will increase the Exercise Price or decrease the number of Warrant Shares as otherwise determined pursuant to this Section 2, provided further that if the Holder does not accept such adjustments as appropriately protecting its interests hereunder against such dilution,

then the Company's board of directors and the Holder shall agree, in good faith, upon an independent investment bank of nationally recognized standing to make such appropriate adjustments, whose determination shall be final and binding and whose fees and expenses shall be borne by the Company.

(e) Floor Exercise Price. Notwithstanding anything to the contrary in this Warrant, in no event shall the Exercise Price be reduced below the Floor Price (subject to appropriate adjustments for any stock dividend, stock split, stock combination, reclassification or similar transaction after the Issuance Date).

Calculations

. All calculations under this Section 2 shall be made by rounding to the nearest cent or the nearest 1/100th of a share, as applicable. The number of shares of Common Stock outstanding at any given time shall not include shares owned or held by or for the account of the Company.

3. RIGHTS UPON DISTRIBUTION OF ASSETS. In addition to any adjustments pursuant to Section 2 above, if the Company shall declare or make any dividend or other distribution of its assets (or rights to acquire its assets) to holders of shares of Common Stock, by way of return of capital or otherwise (including, without limitation, any distribution of cash, stock or other securities, property or options by way of a dividend, spin off, reclassification, corporate rearrangement, scheme of arrangement or other similar transaction) (a "**Distribution**"), at any time after the issuance of this Warrant, then, in each such case, the Holder shall be entitled to participate in such Distribution to the same extent that the Holder would have participated therein if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Maximum Percentage) immediately before the date on which a record is taken for such Distribution, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the participation in such Distribution (provided, however, to the extent that the Holder's right to participate in any such Distributions would result in the Holder exceeding the Maximum Percentage, then the Holder shall not be entitled to participate in such Distribution to such extent (or the beneficial ownership of any such shares of Common Stock as a result of such Distribution to such extent) and such Distribution to such extent shall be held in abeyance for the benefit of the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Maximum Percentage).

4. PURCHASE RIGHTS; FUNDAMENTAL TRANSACTIONS.

(a) Purchase Rights. In addition to any adjustments pursuant to Section 2 above, if at any time the Company grants, issues or sells any Options, Convertible Securities or rights to purchase stock, warrants, securities or other property pro rata to the record holders of any class of shares of Common Stock (the "**Purchase Rights**"), then the Holder will be entitled to acquire, upon the terms applicable to such Purchase Rights, the aggregate Purchase Rights which the Holder could have acquired if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Maximum Percentage) immediately before the date on which a record is taken for the grant, issuance or sale of such Purchase Rights, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to

be determined for the grant, issue or sale of such Purchase Rights (provided, however, to the extent that the Holder's right to participate in any such Purchase Right would result in the Holder exceeding the Maximum Percentage, then the Holder shall not be entitled to participate in such Purchase Right to such extent (or beneficial ownership of such shares of Common Stock as a result of such Purchase Right to such extent) and such Purchase Right to such extent shall be held in abeyance for the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Maximum Percentage).

Fundamental Transactions. The Company shall not enter into or be party to a Fundamental Transaction unless the Successor Entity assumes in writing all of the obligations of the Company under this Warrant in accordance with the provisions of this Section 4(b), including agreements to deliver to the Holder in exchange for this Warrant a security of the Successor Entity evidenced by a written instrument substantially similar in form and substance to this Warrant, including, without limitation, which is exercisable for a corresponding number of shares of capital stock equivalent to the shares of Common Stock acquirable and receivable upon exercise of this Warrant (without regard to any limitations on the exercise of this Warrant) prior to such Fundamental Transaction, and with an exercise price which applies the Exercise Price hereunder to such shares of capital stock (but taking into account the relative value of the shares of Common Stock pursuant to such Fundamental Transaction and the value of such shares of capital stock, such adjustments to the number of shares of capital stock and such exercise price being for the purpose of protecting the economic value of this Warrant immediately prior to the consummation of such Fundamental Transaction). Upon the consummation of any Fundamental Transaction, the Successor Entity shall succeed to, and be substituted for (so that from and after the date of the applicable Fundamental Transaction, the provisions of this Warrant referring to the "Company" shall refer instead to the Successor Entity), and may exercise every right and power of the Company and shall assume all of the obligations of the Company under this Warrant with the same effect as if such Successor Entity had been named as the Company herein. Upon consummation of each Fundamental Transaction, the Successor Entity shall deliver to the Holder confirmation that there shall be issued upon exercise of this Warrant at any time after the consummation of the applicable Fundamental Transaction, in lieu of the shares of Common Stock (or other securities, cash, assets or other property (except such items still issuable under Sections 3 and 4(b) above, which shall continue to be receivable thereafter)) issuable upon the exercise of this Warrant prior to the applicable Fundamental Transaction, such shares of stock (or its equivalent) of the Successor Entity (including its Parent Entity) which the Holder would have been entitled to receive upon the happening of the applicable Fundamental Transaction had this Warrant been exercised immediately prior to the applicable Fundamental Transaction (without regard to any limitations on the exercise of this Warrant, including without limitation, the Maximum Percentage), as adjusted in accordance with the provisions of this Warrant. Notwithstanding the foregoing, and without limiting Section 1(g) hereof, the Holder may elect, at its sole option, by delivery of written notice to the Company to waive this Section 4(b) to permit the Fundamental Transaction without the assumption of this Warrant. In addition to and not in substitution for any other rights hereunder, prior to the consummation of each Fundamental Transaction pursuant to which holders of shares of Common Stock are entitled to receive securities or other assets with respect to or in exchange for shares of Common Stock (a "**Corporate Event**"), the Company shall make appropriate provision to insure that the Holder will thereafter have the right to receive upon an exercise of this Warrant at any time after the consummation of the applicable Fundamental Transaction but prior to the Expiration Date, in

lieu of the shares of the Common Stock (or other securities, cash, assets or other property (except such items still issuable under Sections 3 and 4(b) above, which shall continue to be receivable thereafter)) issuable upon the exercise of the Warrant prior to such Fundamental Transaction , such shares of stock, securities, cash, assets or any other property whatsoever (including warrants or other purchase or subscription rights) which the Holder would have been entitled to receive upon the happening of the applicable Fundamental Transaction had this Warrant been exercised immediately prior to the applicable Fundamental Transaction (without regard to any limitations on the exercise of this Warrant, including without limitation, the Maximum Percentage). Provision made pursuant to the preceding sentence shall be in a form and substance reasonably satisfactory to the Holder.

Notwithstanding the foregoing, in the event of a Change of Control, at the request of the Holder delivered before the 90th day after such Change of Control, the Company (or the Successor Entity) shall purchase this Warrant from the Holder by paying to the Holder, within five Business Days after such request (or, if later, on the effective date of the Change of Control), cash in an amount equal to the Black Scholes Value of the remaining unexercised portion of this Warrant on the date of such Change of Control.

(c) Application. The provisions of this Section 4 shall apply similarly and equally to successive Fundamental Transactions and Corporate Events and shall be applied as if this Warrant (and any such subsequent warrants) were fully exercisable and without regard to any limitations on the exercise of this Warrant (provided that the Holder shall continue to be entitled to the benefit of the Maximum Percentage, applied however with respect to shares of capital stock registered under the 1934 Act and thereafter receivable upon exercise of this Warrant (or any such other warrant)).

5. NONCIRCUMVENTION. The Company hereby covenants and agrees that the Company will not, by amendment of its Certificate of Incorporation, Bylaws or through any reorganization, transfer of assets, consolidation, merger, scheme of arrangement, dissolution, issue or sale of securities, or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, and will at all times in good faith carry out all the provisions of this Warrant and take all action as may be required to protect the rights of the Holder. Without limiting the generality of the foregoing, the Company (i) shall not increase the par value of any shares of Common Stock receivable upon the exercise of this Warrant above the Exercise Price then in effect, (ii) shall take all such actions as may be necessary or appropriate in order that the Company may validly and legally issue fully paid and nonassessable shares of Common Stock upon the exercise of this Warrant, and (iii) shall, so long as this Warrant is outstanding, take all action necessary to reserve and keep available out of its authorized and unissued shares of Common Stock, solely for the purpose of effecting the exercise of this Warrant, 100% of the number of shares of Common Stock issuable upon exercise of this Warrant then outstanding (without regard to any limitations on exercise).

6. WARRANT HOLDER NOT DEEMED A STOCKHOLDER. Except as otherwise specifically provided herein, the Holder, solely in such Person's capacity as a holder of this Warrant, shall not be entitled to vote or receive dividends or be deemed the holder of share capital of the Company for any purpose, nor shall anything contained in this Warrant be construed to confer upon the Holder, solely in such Person's capacity as the Holder of this Warrant, any of the rights of a stockholder of the Company or any right to vote, give or withhold consent to any corporate action (whether any reorganization, issue of stock, reclassification of

stock, consolidation, merger, conveyance or otherwise), receive notice of meetings, receive dividends or subscription rights, or otherwise, prior to the issuance to the Holder of the Warrant Shares which such Person is then entitled to receive upon the due exercise of this Warrant. In addition, nothing contained in this Warrant shall be construed as imposing any liabilities on the Holder to purchase any securities (upon exercise of this Warrant or otherwise) or as a stockholder of the Company, whether such liabilities are asserted by the Company or by creditors of the Company.

7. REISSUANCE OF WARRANTS.

(a) Registration of Warrant. The Company shall register this Warrant, upon the records to be maintained by the Company for that purpose (the "**Warrant Register**"), in the name of the record Holder hereof from time to time. The Company may deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary. The Company shall also register any transfer, exchange, reissuance or cancellation of any portion of this Warrant in the Warrant Register.

(b) Transfer of Warrant . This Warrant may be offered for sale, sold, transferred or assigned without the consent of the Company**,** except as may otherwise be required by applicable securities laws. Subject to applicable securities laws, if this Warrant is to be transferred, the Holder shall surrender this Warrant to the Company, together with all applicable transfer taxes, whereupon the Company will forthwith issue and deliver upon the order of the Holder a new Warrant (in accordance with Section 7(e)), registered as the Holder may request, representing the right to purchase the number of Warrant Shares being transferred by the Holder and, if less than the total number of Warrant Shares then underlying this Warrant is being transferred, a new Warrant (in accordance with Section 7(e)) to the Holder representing the right to purchase the number of Warrant Shares not being transferred. The acceptance of the new Warrant by the transferee thereof shall be deemed the acceptance by such transferee of all of the rights and obligations in respect of the new Warrant that the Holder has in respect of this Warrant.

(c) Lost, Stolen or Mutilated Warrant. Upon receipt by the Company of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant, and, in the case of loss, theft or destruction, of any indemnification undertaking by the Holder to the Company in customary form and, in the case of mutilation, upon surrender and cancellation of this Warrant, the Company shall execute and deliver to the Holder a new Warrant (in accordance with Section 7(e)) representing the right to purchase the Warrant Shares then underlying this Warrant.

(d) Exchangeable for Multiple Warrants. This Warrant is exchangeable, upon the surrender hereof by the Holder at the principal office of the Company, for a new Warrant or warrants (in accordance with Section 7(e)) representing in the aggregate the right to purchase the number of Warrant Shares then underlying this Warrant, and each such new Warrant will represent the right to purchase such portion of such Warrant Shares as is designated by the Holder at the time of such surrender; provided, however, that no warrants for fractional shares of Common Stock shall be given.

(e) Issuance of New Warrant. Whenever the Company is required to issue a new Warrant pursuant to the terms of this Warrant, such new Warrant (i) shall be of like tenor with this Warrant, (ii) shall represent, as indicated on the face of such new Warrant, the right to purchase the Warrant Shares then underlying this Warrant (or in the case of a new Warrant being issued pursuant to Section 7(b) or Section 7(c), the Warrant Shares designated by the Holder which, when added to the number of shares of Common Stock underlying the other new Warrant(s) issued in connection with such issuance, does not exceed the number of Warrant Shares then underlying this Warrant), (iii) shall have an issuance date, as indicated on the face of such new Warrant which is the same as the Issuance Date, and (iv) shall have the same rights and conditions as this Warrant.

8. NOTICES. (a) Any and all notices or other communications or deliveries required or permitted to be provided hereunder shall be in writing and shall be deemed given and effective on the earliest of: (a) the date of transmission, if such notice or communication is delivered via email at the email address set forth on the signature pages attached hereto (or otherwise provided below) or facsimile at the facsimile number set forth on the signature pages attached hereto at or prior to 5:30 p.m. (New York City time) on a Trading Day, (b) the next Trading Day after the date of transmission, if such notice or communication is delivered via email at the email address set forth on the signature pages attached hereto (or otherwise provided below) or facsimile at the facsimile number set forth on the signature pages attached hereto on a day that is not a Trading Day or later than 5:30 p.m. (New York City time) on any Trading Day, (c) the second (2 nd) Trading Day following the date of mailing, if sent by U.S. nationally recognized overnight courier service or (d) upon actual receipt by the party to whom such notice is required to be given. The addresses for such communications shall be:

If to the Company:

Threshold Pharmaceuticals, Inc.
170 Harbor Way, Suite 300
South San Francisco, CA 94080
Fax: (650) 474-XXXX
Attention: Chief Executive Officer
email: BSelick@thresholdpharm.com

With copy to:

Cooley LLP
101 California Street, 5th Floor
San Francisco, CA 94111
Fax: (415) 693-2222
Attention: Chadwick L. Mills, Esq.
email: cmills@cooley.com

If to the Holder:

To the address, email address or facsimile number set forth in the Warrant Register, or as otherwise provided by the Holder to the Company in accordance with this Section 8.

(b) The Company shall provide the Holder with prompt written notice of all actions taken pursuant to this Warrant, including in reasonable detail a description of such action and the reason therefor. Without limiting the generality of the foregoing, the Company will give written notice to the Holder (i) immediately upon each adjustment of the Exercise Price and the number of Warrant Shares, setting forth in reasonable detail, and certifying, the calculation of such adjustment(s) and (ii) at least fifteen (15) days prior to the date on which the Company closes its books or takes a record (A) with respect to any dividend or distribution upon the shares of Common Stock, (B) with respect to any grants, issuances or sales of any Options, Convertible Securities or rights to purchase stock, warrants, securities or other property pro rata to the record holders of any class of shares of Common Stock or (C) for determining rights to vote with respect to any Fundamental Transaction, dissolution or liquidation, provided in each case that such information shall be made known to the public prior to or in conjunction with such notice being provided to the Holder.

9. AMENDMENT AND WAIVER. Except as otherwise provided herein, the provisions of this Warrant may be amended and the Company may take any action herein prohibited, or omit to perform any act herein required to be performed by it, only if the Company has obtained the written consent of the Holder.

10. SEVERABILITY. If any provision of this Warrant is prohibited by law or otherwise determined to be invalid or unenforceable by a court of competent jurisdiction, the provision that would otherwise be prohibited, invalid or unenforceable shall be deemed amended to apply to the broadest extent that it would be valid and enforceable, and the invalidity or unenforceability of such provision shall not affect the validity of the remaining provisions of this Warrant so long as this Warrant as so modified continues to express, without material change, the original intentions of the parties as to the subject matter hereof and the prohibited nature, invalidity or unenforceability of the provision(s) in question does not substantially impair the respective expectations or reciprocal obligations of the parties or the practical realization of the benefits that would otherwise be conferred upon the parties. The parties will endeavor in good faith negotiations to replace the prohibited, invalid or unenforceable provision(s) with a valid provision(s), the effect of which comes as close as possible to that of the prohibited, invalid or unenforceable provision(s).

11. GOVERNING LAW. This Warrant shall be governed by and construed and enforced in accordance with, and all questions concerning the construction, validity, interpretation and performance of this Warrant shall be governed by, the internal laws of the State of York, without giving effect to any choice of law or conflict of law provision or rule (whether of the State of New York or any other jurisdictions) that would cause the application of the laws of any jurisdictions other than the State of New York. The Company hereby irrevocably submits to the exclusive jurisdiction of the state and federal courts sitting in The City of New York, Borough of Manhattan, for the adjudication of any dispute hereunder or in connection

herewith or with any transaction contemplated hereby or discussed herein, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law. Nothing contained herein shall be deemed or operate to preclude the Holder from bringing suit or taking other legal action against the Company in any other jurisdiction to collect on the Company's obligations to the Holder or to enforce a judgment or other court ruling in favor of the Holder. **THE COMPANY HEREBY IRREVOCABLY WAIVES ANY RIGHT IT MAY HAVE TO, AND AGREES NOT TO REQUEST, A JURY TRIAL FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION WITH OR ARISING OUT OF THIS WARRANT OR ANY TRANSACTION CONTEMPLATED HEREBY.**

12. CONSTRUCTION; HEADINGS. This Warrant shall be deemed to be jointly drafted by the Company and the Holder and shall not be construed against any Person as the drafter hereof. The headings of this Warrant are for convenience of reference and shall not form part of, or affect the interpretation of, this Warrant.

13. DISPUTE RESOLUTION. In the case of a dispute as to the determination of the Exercise Price, the Closing Sale Price, the Closing Bid Price or fair market value or the arithmetic calculation of the Warrant Shares (as the case may be), the Company or the Holder (as the case may be) shall submit the disputed determinations or arithmetic calculations (as the case may be) via email or facsimile (i) within two (2) Business Days after receipt of the applicable notice giving rise to such dispute to the Company or the Holder (as the case may be) or (ii) if no notice gave rise to such dispute, at any time after the Company or the Holder (as the case may be) learned of the circumstances giving rise to such dispute (including, without limitation, as to whether any issuance or sale or deemed issuance or sale was an issuance or sale or deemed issuance or sale of Excluded Securities). If the Holder and the Company are unable to agree upon such determination or calculation (as the case may be) of the Exercise Price, the Closing Sale Price, the Closing Bid Price or fair market value or the number of Warrant Shares (as the case may be) within five (5) Business Days of such disputed determination or arithmetic calculation being submitted to the Company or the Holder (as the case may be), then the Company shall, within two (2) Business Days submit via email or facsimile (a) the disputed determination of the Exercise Price, the Closing Sale Price, the Closing Bid Price or fair market value (as the case may be) to an independent, reputable investment bank selected by the Holder or (b) the disputed arithmetic calculation of the Warrant Shares to the Company's independent, outside accountant. The Company shall cause the investment bank or the accountant (as the case may be) to perform the determinations or calculations (as the case may be) and notify the Company and the Holder of the results no later than ten (10) Business Days from the time it receives such disputed determinations or calculations (as the case may be). Such investment bank's or accountant's determination or calculation (as the case may be) shall be binding upon all parties absent demonstrable error. The expenses of the investment bank and accounting will be borne by the Company unless the investment bank or accountant determines that the determination of the Exercise Price, the Closing Sale Price, the Closing Bid Price or fair market value or the number of Warrant Shares (as the case may be) by the Holder was incorrect, in which case the expense of the investment bank and accountant will be borne by the Holder.

14. REMEDIES, CHARACTERIZATION, OTHER OBLIGATIONS, BREACHES AND INJUNCTIVE RELIEF. The remedies provided in this Warrant shall be cumulative and in addition to all other remedies available under this Warrant, at law or in equity (including a decree of specific performance and/or other injunctive relief), and nothing herein shall limit the right of the Holder to pursue actual damages for any failure by the Company to comply with the terms of this Warrant. The Company acknowledges that a breach by it of its obligations hereunder may cause irreparable harm to the Holder and that the remedy at law for any such breach may be inadequate. The Company therefore agrees that, in the event of any such breach or threatened breach, the holder of this Warrant shall be entitled to seek, in addition to all other available remedies, an injunction restraining any breach without any bond or other security being required. The Company shall provide all information and documentation to the Holder that is reasonably requested by the Holder to enable the Holder to confirm the Company's compliance with the terms and conditions of this Warrant (including, without limitation, compliance with Section 2hereof). Notwithstanding the foregoing or anything else herein to the contrary, other than as expressly provided in Section 1(c) or 1(d) hereof, if the Company is for any reason unable to issue and deliver Warrant Shares upon exercise of this Warrant as required pursuant to the terms hereof, the Company shall have no obligation to pay to the Holder any cash or other consideration or otherwise "net cash settle" this Warrant.

15. FORCED EXERCISE. If at any time from and after ninety (90) days following the Adjustment Date (the "**Forced Exercise Eligibility Date**"), (i) the arithmetic average of the VWAP of the Common Stock for any twenty (20) consecutive Trading Days that commences on or after the Forced Exercise Eligibility Date (the "**Forced Exercise Measuring Period**") equals or exceeds $18.00 (subject to appropriate adjustments for any stock dividend, stock split, stock combination, reclassification or similar transaction after the Issuance Date) and (ii) there is not then an Equity Conditions Failure, the Company shall have the right to require the Holder to exercise all or any portion of the unexercised portion of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Maximum Percentage), in each case as designated in the Forced Exercise Notice (as defined below) into fully paid, validly issued and nonassessable shares of Common Stock in accordance with Section 1(a) hereof (or, solely if a registration statement registering the issuance of the Warrant Shares under the Securities Act is not then effective or available for the issuance of the Warrant Shares, in accordance with Section 1(a) and 1(d) hereof) at the Exercise Price as of the Forced Exercise Date (as defined below) (a "**Forced Exercise**"). The Company may exercise its right to require Forced Exercise under this Section 15 by delivering, within not more than two (2) Trading Days following the end of such Forced Exercise Measuring Period, a written notice thereof by facsimile and overnight courier to all of, but not less than all, of the Holder and the holders of the Other Warrants and the Transfer Agent (the "**Forced Exercise Notice**" and the date all of the holders of the Warrants received such notice by facsimile is referred to as the "**Forced Exercise Notice Date**"). The Forced Exercise Notice shall be irrevocable. The Forced Exercise Notice shall (x) state (A) the Trading Day selected for the Forced Exercise, which Trading Day shall be no sooner than five (5) Trading Days nor later than ten (10) Trading Days following the Forced Exercise Notice Date (the "**Forced Exercise Date**"), and (B) the aggregate number of Warrant Shares subject to Forced Exercise from the Holder (the "**Forced Exercise Share Number**") and all of the holders of the Other Warrants pursuant to this Section 15 (the "**Holders' Aggregate Forced Exercise Share Number**") (and analogous provisions under the Other Warrants); and (y) certify that there has been no Equity Conditions Failure. If the Equity

Conditions were satisfied as of the Forced Exercise Notice Date, but the Equity Conditions are no longer satisfied at any time prior to the Forced Exercise Date, the Company shall provide the Holder a subsequent notice to that effect indicating that unless the Holder waives the Equity Conditions, the Forced Exercise Notice shall be void *ab initio* and of no further force or effect. The Company shall deliver to the Holder a notice no later than 10:00 a.m., New York time, on the Forced Exercise Date which notice shall certify whether or not the Equity Conditions have been satisfied. Notwithstanding the foregoing, nothing in this subsection shall prevent the Holder from exercising this Warrant, in whole or part, on or prior to the Forced Exercise Date. The Company covenants and agrees that it will honor all Exercise Notices tendered from the time of delivery of the Forced Exercise Notice through the Forced Exercise Date. Upon an Equity Conditions Failure, the Holder may revoke any Exercise Notice delivered after the Forced Exercise Notice is received by the Holder and the Company, within one (1) Business Day of such revocation, shall return the Aggregate Exercise Price applicable to any such Exercise Notice(s) to the Holder by wire transfer of immediately available funds and any Warrants so exercised shall be deemed reinstated and returned to the Holders, if applicable.

16. CERTAIN DEFINITIONS. For purposes of this Warrant, the following terms shall have the following meanings:

(a) "**Adjustment Right**" means any right granted with respect to any securities issued in connection with, or with respect to, any issuance or sale (or deemed issuance or sale in accordance with Section 2) of shares of Common Stock (other than rights of the type described in Section 3 and 4 hereof) that could result in a decrease in the net consideration received by the Company in connection with, or with respect to, such securities (including, without limitation, any cash settlement rights, cash adjustment or other similar rights).

(b) "**Black Scholes Value** " means the value of the unexercised portion of this Warrant remaining on the date of the Holder's request, which value is calculated using the Black Scholes Option Pricing Model obtained from the "OV" function on Bloomberg utilizing (i) an underlying price per share equal to the greater of (1) the highest Closing Sale Price of the Common Stock during the period beginning on the Trading Day immediately preceding the public disclosure of the applicable Change of Control and ending on the Trading Day immediately preceding the consummation of the applicable Change of Control and (2) the sum of the price per share being offered in cash in the applicable Change of Control (if any) plus the value of the non-cash consideration being offered in the applicable Fundamental Transaction (if any), (ii) a strike price equal to the Exercise Price in effect on the of date of the Holder's request, (iii) a risk-free interest rate corresponding to the U.S. Treasury rate for a period equal to the greater of (1) the remaining term of this Warrant as of the date of the Holder's request and (2) the remaining term of this Warrant as of the date of consummation of the applicable Change of Control or as of the date of the Holder's request pursuant to Section 4(b) if such request is prior to the date of the consummation of the applicable Change of Control and (iv) an expected volatility equal to the lesser of 65% and the 30 day volatility obtained from the HVT function on Bloomberg (determined utilizing a 365 day annualization factor) as of and including the Trading Day immediately following the earlier to occur of the public disclosure or consummation of the applicable Change of Control.

(c) "**Bloomberg**" means Bloomberg, L.P.

(d) "**Business Day**" means any day other than Saturday, Sunday or other day on which commercial banks in The City of New York are authorized or required by law to remain closed.

(e) "**Change of Control**" means any Fundamental Transaction other than (i) any reorganization, recapitalization or reclassification of the Common Stock in which holders of the Company's voting power immediately prior to such reorganization, recapitalization or reclassification continue after such reorganization, recapitalization or reclassification to hold publicly traded securities and, directly or indirectly, the voting power of the surviving entity or entities necessary to elect a majority of the members of the board of directors (or their equivalent if other than a corporation) of such entity or entities, or (ii) pursuant to a migratory merger effected solely for the purpose of changing the jurisdiction of incorporation of the Company.

(f) "**Closing Bid Price**" and "**Closing Sale Price**" means, for any security as of any date, the last closing bid price and last closing trade price, respectively, for such security on the Principal Market, as reported by Bloomberg, or, if the Principal Market begins to operate on an extended hours basis and does not designate the closing bid price or the closing trade price, as the case may be, then the last bid price or the last trade price, respectively, of such security prior to 4:00:00 p.m., New York time, as reported by Bloomberg, or, if the Principal Market is not the principal securities exchange or trading market for such security, the last closing bid price or last trade price, respectively, of such security on the principal securities exchange or trading market where such security is listed or traded as reported by Bloomberg, or if the foregoing do not apply, the last closing bid price or last trade price, respectively, of such security in the over-the-counter market on the electronic bulletin board for such security as reported by Bloomberg, or, if no closing bid price or last trade price, respectively, is reported for such security by Bloomberg, the average of the bid prices, or the ask prices, respectively, of any market makers for such security as reported in the "pink sheets" by Pink Sheets LLC (formerly the National Quotation Bureau, Inc.). If the Closing Bid Price or the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Bid Price or the Closing Sale Price, as the case may be, of such security on such date shall be the fair market value as mutually determined by the Company and the Holder. All such determinations to be appropriately adjusted for any stock dividend, stock split, stock combination or other similar transaction during the applicable calculation period.

(g) "**Common Stock**" means (i) the Company's shares of common stock, and (ii) any capital stock into which such common stock shall have been changed or any share capital resulting from a reclassification of such common stock.

(h) "**Convertible Securities**" means any stock or other security (other than Options) that is at any time and under any circumstances, directly or indirectly, convertible into, exercisable or exchangeable for, or which otherwise entitles the holder thereof to acquire, any shares of Common Stock.

(i) "**Data Release Date**" means the first to occur of (i) the last to occur of (x) the date on which top-line efficacy data from the Company's TH-CR 406 trial, a Phase 3 clinical trial of TH-302 plus doxorubicin versus doxorubicin alone in patients with

locally advanced unresectable or metastatic soft tissue sarcoma is first publicly announced in a press release issued by the Company and (y) the date on which top-line efficacy data from the MAESTRO study, a Phase 3 clinical trial of TH-302 in combination with gemcitabine in patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma is first publicly announced in a press release issued by the Company and (ii) the second anniversary of the Issuance Date of this Warrant.

(j) "**Eligible Market**" means The New York Stock Exchange, the NYSE Amex, the Nasdaq Global Select Market, the Nasdaq Global Market or the Principal Market.

(k) "**Equity Conditions**" means: (i) on each day during the period beginning thirty (30) Trading Days prior to the applicable date of determination and ending on and including the applicable date of determination (the "**Equity Conditions Measuring Period**"), all shares of Common Stock issued and issuable upon exercise of the Warrants shall be eligible for sale without restriction or limitation and without the need for registration under any applicable federal or state securities laws, unless in each such case such Warrant Shares are held by or issuable to an affiliate of the Company within the meaning of Rule 144 promulgated under the Securities Act; (ii) on each day during the Equity Conditions Measuring Period, the Common Stock is listed or designated for quotation on the Principal Market or an Eligible Market and shall not have been suspended from trading from the Principal Market or Eligible Market on which the Common Stock is primarily listed on and quoted for trading (the "**Primary Market**") any applicable exchanges or markets (other than suspensions of not more than two (2) days and occurring prior to the applicable date of determination due to business announcements by the Company) nor shall proceedings for such delisting or suspension from the Principal Market have been commenced, threatened or pending either (1) in writing by the Principal Market or (2) by falling below the minimum listing maintenance requirements of all relevant exchanges and markets unless, in the case of clause (1) or (2) above, (x) the Company shall meet all minimum initial listing conditions of one or more other Eligible Markets or (y) the commenced, threatened or pending delisting or suspension is due to the applicable price of the Common Stock falling below a listing standard provided the Company is actively taking the necessary steps to effect a reverse stock split to meet the requirements of such Eligible Market or the price of the Common Stock has risen such that the commenced, threatened or pending delisting or suspension is no longer applicable; and (iii) on each day during the Equity Conditions Measuring Period, the Company shall have delivered Common Stock upon exercise of this Warrant to the Holder on a timely basis as set forth in Section 1(a) hereof or shall have otherwise timely satisfied its obligations under Section 1(c) hereof, unless in each such case the Company's failure to timely deliver or otherwise satisfy such obligations is due solely to any action or inaction by the Holder; (iv) on each day during the Equity Conditions Measuring Period, no public announcement of a pending, proposed or intended Fundamental Transaction shall have occurred which has not been abandoned, terminated or consummated; (v) the Holder shall not be in possession of any material, non-public information provided to the Holder by the Company, any of its affiliates or any of their respective officers, employees, directors, representatives, or agents; and (vi) on each day during the Equity Conditions Measuring Period, the Company shall not be in breach of any material term or condition of this Warrant.

(l) "**Equity Conditions Failure**" means that during the period beginning with the first Trading Day of the Forced Exercise Measuring Period through the applicable Forced Exercise Notice Date or Forced Exercise Date, as the case may be, the Equity Conditions have not been satisfied (or waived in writing by the Holder).

(m) "**Excluded Securities**" means the issuance of (a) shares of Common Stock or options to employees, officers or directors of the Company in their capacity as such pursuant to any stock or option plan or employment agreement duly adopted for such purpose, by a majority of the non-employee members of the Board of Directors or a majority of the members of a committee of non-employee directors established for such purpose, (b) securities upon the exercise or exchange of or conversion of the securities issued hereunder and/or other securities exercisable or exchangeable for or convertible into shares of Common Stock issued and outstanding on the date of this Agreement, provided that such securities have not been amended since the date of this Agreement to increase the number of such securities or to decrease the exercise price, exchange price or conversion price of such securities, and (c) securities issued pursuant to acquisitions or strategic transactions approved by a majority of the disinterested directors of the Company, provided that any such issuance shall only be to a Person (or to the equity holders of a Person) which is, itself or through its subsidiaries, an operating company or an owner of an asset in a business synergistic with the business of the Company and shall provide to the Company additional benefits in addition to the investment of funds, but shall not include a transaction in which the Company is issuing securities primarily for the purpose of raising capital or to an entity whose primary business is investing in securities.

(n) "**Expiration Date**" means the date that is the fifth (5th) anniversary of the Issuance Date, if such date falls on a day other than a Business Day or on which trading does not take place on the Principal Market (a "**Holiday**"), the next date that is not a Holiday.

(o) "**Fundamental Transaction**" means that (i) the Company or any of its direct or indirect wholly-owned subsidiaries shall, directly or indirectly, in one or more related transactions, (A) consolidate or merge with or into (whether or not the Company or any of its subsidiaries is the surviving corporation) any other Person, or (B) sell, lease, license, assign, transfer, convey or otherwise dispose of all or substantially all of its respective properties or assets to any other Person, or (C) allow any other Person to make a purchase, tender or exchange offer that is accepted by the holders of more than 50% of the outstanding shares of Voting Stock of the Company (not including any shares of Voting Stock of the Company held by the Person or Persons making or party to, or associated or affiliated with the Persons making or party to, such purchase, tender or exchange offer), or (D) consummate a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with any other Person whereby such other Person acquires more than 50% of the outstanding shares of Voting Stock of the Company (not including any shares of Voting Stock of the Company held by the other Person or other Persons making or party to, or associated or affiliated with the other Persons making or party to, such stock or share purchase agreement or other business combination), or (E) reorganize, recapitalize or reclassify the Common Stock, or (ii) any "person" or "group" (as these terms are used for purposes of Sections 13(d) and 14(d) of the 1934 Act and the rules and regulations promulgated thereunder) is or shall become the "beneficial owner" (as defined in Rule 13d-3 under the 1934

Act), directly or indirectly, of 50% of the aggregate ordinary voting power represented by issued and outstanding Voting Stock of the Company.

(p) "**Market Price**" means the arithmetic average of the VWAP for the Common Stock on each of the twenty (20) Trading Days immediately preceding the applicable date.

(q) "**Option Value**" means the value of the applicable Option or Convertible Security (as the case may be) as of the date of issuance thereof calculated using the Black Scholes Option Pricing Model obtained from the "OV" function on Bloomberg utilizing (i) an underlying price per share equal to the Closing Sale Price of the Common Stock on the Trading Day immediately preceding the public announcement of the execution of definitive documents with respect to the issuance of such Option or Convertible Security (as the case may be), (ii) a risk-free interest rate corresponding to the U.S. Treasury rate for a period equal to the remaining term of such Option or Convertible Security (as the case may be) as of the date of issuance of such Option or Convertible Security (as the case may be) and (iii) an expected volatility equal to the lesser of 65% and the 30 day volatility obtained from the HVT function on Bloomberg (determined utilizing a 365 day annualization factor) as of and including the Trading Day immediately following the date of issuance of such Option or Convertible Security (as the case may be)

(r) "**Options**" means any rights, warrants or options to subscribe for or purchase shares of Common Stock or Convertible Securities.

(s) "**Parent Entity**" of a Person means an entity that, directly or indirectly, controls the applicable Person and whose common stock or equivalent equity security is quoted or listed on an Eligible Market, or, if there is more than one such Person or Parent Entity, the Person or Parent Entity with the largest public market capitalization as of the date of consummation of the Fundamental Transaction.

(t) "**Person**" means an individual, a limited liability company, a partnership, a joint venture, a corporation, a trust, an unincorporated organization, any other entity or a government or any department or agency thereof.

(u) "**Principal Market**" means the Nasdaq Capital Market.

(v) "**Successor Entity**" means the Person (or, if so elected by the Holder, the Parent Entity) formed by, resulting from or surviving any Fundamental Transaction or the Person (or, if so elected by the Holder, the Parent Entity) with which such Fundamental Transaction shall have been entered into.

(w) "**Trading Day**" means any day on which the Common Stock is traded on the Principal Market, or, if the Principal Market is not the principal trading market for the Common Stock, then on the principal securities exchange or securities market on which the Common Stock is then traded, provided that "Trading Day" shall not include any day on which the Common Stock is scheduled to trade on such exchange or market for less than 4.5 hours or any day that the Common Stock is suspended from trading during the final hour of trading on such exchange or market (or if such exchange or market does not designate in advance the

closing time of trading on such exchange or market, then during the hour ending at 4:00:00 p.m., New York time).

(x) "**Voting Stock**" of a Person means capital stock of such Person of the class or classes pursuant to which the holders thereof have the general voting power to elect, or the general power to appoint, at least a majority of the board of directors, managers or trustees of such Person (irrespective of whether or not at the time capital stock of any other class or classes shall have or might have voting power by reason of the happening of any contingency).

(y) "**VWAP**" means, for any security as of any date, the dollar volume-weighted average price for such security on the Principal Market (or, if the Principal Market is not the principal trading market for such security, then on the principal securities exchange or securities market on which such security is then traded) during the period beginning at 9:30:01 a.m., New York time, and ending at 4:00:00 p.m., New York time, as reported by Bloomberg through its "Volume at Price" function or, if the foregoing does not apply, the dollar volume-weighted average price of such security in the over-the-counter market on the electronic bulletin board for such security during the period beginning at 9:30:01 a.m., New York time, and ending at 4:00:00 p.m., New York time, as reported by Bloomberg, or, if no dollar volume-weighted average price is reported for such security by Bloomberg for such hours, the average of the highest closing bid price and the lowest closing ask price of any of the market makers for such security as reported in the "pink sheets" by OTC Markets Group Inc. (formerly Pink Sheets LLC). If VWAP cannot be calculated for such security on such date on any of the foregoing bases, the VWAP of such security on such date shall be the fair market value as mutually determined by the Company and the Holder. If the Company and the Holder are unable to agree upon the fair market value of such security, then such dispute shall be resolved in accordance with the procedures in Section 13. All such determinations shall be appropriately adjusted for any stock splits, stock dividends, stock combinations, recapitalizations or other similar transactions during such period.

(z) "**Warrants**" means, collectively, this Warrant and the Other Warrants.

[*signature page follows*]

IN WITNESS WHEREOF, the Company has caused this Warrant to Purchase Common Stock to be duly executed as of the Issuance Date set out above.

THRESHOLD PHARMACEUTICALS, INC

By:
Name:
Title:

EXHIBIT A

EXERCISE NOTICE
TO BE EXECUTED BY THE REGISTERED HOLDER TO EXERCISE THIS
WARRANT TO PURCHASE COMMON STOCK

THRESHOLD PHARMACEUTICALS, INC.

The undersigned holder hereby exercises the right to purchase _____ of the shares of Common Stock ("**Warrant Shares**") of **THRESHOLD PHARMACEUTICALS, INC**, a Delaware corporation (the "**Company**"), evidenced by the attached Warrant to Purchase Common Stock (the "**Warrant**"). Capitalized terms used herein and not otherwise defined shall have the respective meanings set forth in the Warrant.

1. Form of Exercise Price. The Holder intends that payment of the Exercise Price shall be made as:

_____a "Cash Exercise" with respect to _____ Warrant Shares; and/or

_____a "Cashless Exercise" with respect to _____ Warrant Shares (eligible for use only in accordance with Section 1(d) of the Warrant).

2. Payment of Exercise Price. In the event that the holder has elected a Cash Exercise with respect to some or all of the Warrant Shares to be issued pursuant hereto, the holder shall pay the Aggregate Exercise Price in the sum of $_____ to the Company in accordance with the terms of the Warrant.

3. Delivery of Warrant Shares. The Company shall deliver to the holder _____ Warrant Shares in accordance with the terms of the Warrant. If the shares are to be delivered electronically, please complete the DTC DWAC information below.

3. Representation and Warranties. By its delivery of this Exercise Notice, the undersigned represents and warrants to the Company that in giving effect to the exercise evidenced hereby, the Holder will not beneficially own in excess of the number of shares of Common Stock (determined in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended) permitted to be owned under Section 1(f) of the Warrant to which this notice relates.

Date: _____ __, _____

Name of Registered Holder

By:
Name:
Title:

ACKNOWLEDGMENT

The Company hereby acknowledges this Exercise Notice and hereby directs [INSERT NAME OF TRANSFER AGENT] to issue the above indicated number of shares of Common Stock in accordance with the Transfer Agent Instructions dated _____, 201_ from the Company and acknowledged and agreed to by [INSERT NAME OF TRANSFER AGENT].

THRESHOLD PHARMACEUTICALS, INC

By:
Name:
Title:

Exhibit 10.14

THRESHOLD PHARMACEUTICALS, INC.

CHANGE OF CONTROL SEVERANCE AGREEMENT

The Change of Control Severance Agreement (the "Agreement") is made and entered into effective as of _____the ("Effective Date"), by and between _____ (the "Employee") and Threshold Pharmaceuticals, Inc., a Delaware corporation (the "Company"). Certain capitalized terms used in this Agreement are defined in Section 1 below.

RECITALS

A. It is expected that the Company from time to time will consider the possibility of a Change of Control. The Board of Directors of the Company (the "Board") recognizes that such consideration can be a distraction to the Employee and can cause the Employee to consider alternative employment opportunities.

B. The Board believes that it is in the best interests of the Company and its stockholders to provide the Employee with an incentive to continue Employee's employment and to maximize the value of the Company upon a Change of Control for the benefit of its stockholders.

C. In order to provide the Employee with enhanced financial security and sufficient encouragement to remain with the Company notwithstanding the possibility of a Change of Control, the Board believes that it is imperative to provide the Employee with certain severance benefits upon the Employee's termination of employment following a Change of Control.

AGREEMENT

In consideration of the mutual covenants herein contained and the continued employment of Employee by the Company, the parties agree as follows:

1. Definition of Terms. The following terms referred to in this Agreement shall have the following meanings:

(a) Cause. "Cause" shall mean (i) Employee's gross negligence or willful failure substantially to perform his or her duties and responsibilities to the Company or deliberate violation of a Company policy; (ii) Employee's commission of any act of fraud, embezzlement, dishonesty or any other willful misconduct that has caused or is reasonably expected to result in material injury to the Company; (iii) unauthorized use or disclosure by Employee of any proprietary information or trade secrets of the Company or any other party to whom the Employee owes an obligation of nondisclosure as a result of his or her relationship with the Company; or (iv) Employee's willful breach of any of his or her obligations under any written agreement or covenant with the Company. The determination as to whether an Employee is being terminated for Cause shall be made in good faith by the Company and shall be final and binding on the Employee.

(b) Change of Control. "Change of Control" shall mean the occurrence of any of the following events:

(i) the approval by stockholders of the Company of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) more than fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity outstanding immediately after such merger or consolidation;

(ii) the approval by the stockholders of the Company of a plan of complete liquidation of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company's assets; or

(iii) any "person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becoming the "beneficial owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of the Company representing 50% or more of the total voting power represented by the Company's then outstanding voting securities.

(c) Involuntary Termination. "Involuntary Termination" shall mean (i) without the Employee's express written consent, a material reduction of the Employee's duties, position or responsibilities relative to the Employee's duties, position or responsibilities in effect immediately prior to such reduction, or the removal of the Employee from such position, duties and responsibilities, unless the Employee is provided with comparable or greater duties, position and responsibilities; (ii) without the Employee's express written consent, a material reduction by the Company of the Employee's base salary as in effect immediately prior to such reduction; (iii) without the Employee's express written consent, the imposition of a requirement for the relocation of the Employee to a facility or a location more than fifty (50) miles from the Employee's current work location; (iv) any purported termination of the Employee's employment by the Company which is not effected for Cause or for which the grounds relied upon are not valid; or (v) the failure of the Company to obtain the assumption of this Agreement by any successors contemplated in Section 6 below. In order to be considered an Involuntary Termination with regards to parts (i)-(iii) and (v) of this Section 1(c), (1) the Employee's termination from employment must have occurred within six (6) months following the initial existence of the condition giving rise to the Involuntary Termination, (2) within thirty (30) days following the initial existence of the condition giving rise to the Involuntary Termination, the Employee must have provided the Company with notice of the existence of such condition pursuant to Section 8(b), and (3) upon receipt of the notice of the condition from Employee, the Company failed to cure the condition within thirty (30) days.

(d) Termination Date. "Termination Date" shall mean the effective date of any notice of termination delivered by one party to the other hereunder.

2. Term of Agreement. This Agreement shall terminate on the date that all obligations of the parties hereto under this Agreement have been satisfied.

3. At-Will Employment. The Company and the Employee acknowledge that the Employee's employment is and shall continue to be at-will, as defined under applicable law. If the Employee's employment terminates for any reason, the Employee shall not be entitled to any payments, benefits, damages, awards or compensation other than as provided by this Agreement, or as may otherwise be established under the Company's then existing employee benefit plans or policies at the time of termination.

4. Severance Benefits.

(a) Termination Following a Change of Control. If the Employee's employment with the Company terminates as a result of an Involuntary Termination at any time within eighteen (18) months after a Change of Control, and the Employee signs and does not revoke the release of claims pursuant to Section 7 hereto, then subject to Section 4(c), Employee shall be entitled to the following severance benefits:

(1) Twelve (12) months of Employee's base salary and any applicable allowances as in effect as of the date of the termination or, if greater, as in effect immediately prior to the Change of Control, plus an amount equal to the full amount of Employee's target bonus for the calendar year of the date of termination, or, if no target bonus has been established, an amount equal to Employee's target bonus in the prior year, less applicable withholding, payable in a lump sum within sixty (60) days following the date of termination;

(2) unless provided otherwise in the applicable award agreement, the vesting of all equity awards granted by the Company to the Employee prior to the Change of Control shall accelerate and become fully vested to the extent such equity awards are outstanding and unvested at the time of such termination;

(3) the Employee shall be permitted to exercise all vested (including shares that vest as a result of this Agreement) stock options granted by the Company to the Employee prior to the Change of Control for a period ending on the earlier of (i) two (2) years following the Termination Date and (ii) the expiration of the term of the stock options specified in the applicable option agreements; and

(4) the same level of Company-paid health (i.e., medical, vision and dental) coverage and benefits for such coverage as in effect for the Employee (and any eligible dependents) on the day immediately preceding the Employee's Termination Date; provided, however, that (i) the Employee constitutes a qualified beneficiary, as defined in Section 4980B(g)(1) of the Internal Revenue Code of 1986, as amended (the "Code"); and (ii) Employee elects continuation coverage pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), within the time period prescribed pursuant to COBRA. The Company shall continue to provide Employee with such Company-paid coverage on a monthly basis following the Termination Date until the earlier of (i) the date

Employee (and his/her eligible dependents) is no longer eligible to receive continuation coverage pursuant to COBRA, or (ii) twelve (12) months from the Termination Date.

(b) Accrued Wages and Vacation, Expenses. Without regard to the reason for, or the timing of, Employee's termination of employment: (i) the Company shall pay the Employee any unpaid base salary due for periods prior to the Termination Date; (ii) the Company shall pay the Employee all of the Employee's accrued and unused vacation through the Termination Date; and (iii) following submission of proper expense reports by the Employee, the Company shall reimburse the Employee for all expenses reasonably and necessarily incurred by the Employee in connection with the business of the Company prior to the Termination Date. With respect to parts (i) and (ii) of this Section 4(b), payments shall be made as soon as practicable, but no later than March 15th of the calendar year following Employee's termination of employment. Reimbursements made pursuant to part (iii) of this Section 4(b) shall be made as soon as practicable, but no later than December 31st of the year following the calendar year in which such expense was incurred.

(c) Section 409A. Notwithstanding anything to the contrary in this Agreement, if any benefit provided under this Agreement is subject to Section 409A of the Code and such benefit otherwise is payable in connection with the Employee's termination of employment, then the following will apply:

(i) such benefit will not be payable unless such termination constitutes a "separation from service" (as such term is defined in Treasury Regulations Section 1.409A-1(h) without regard to any alternative definition thereunder) ("Separation from Service");

(ii) if the Employee's Separation from Service occurs at a time during the calendar year when the release of claims described in Section 7 could become effective in the calendar year following the calendar year in which such Separation from Service occurs, then for purposes of such benefit, the release of claims will not be deemed effective any earlier than the latest permitted effective date set forth therein (which date, in all cases, will be in the subsequent calendar year); and

(iii) if the Employee is a "specified employee" (as determined in accordance with Section 409A of the Code and related Treasury guidance and regulations) as of the date of the Employee's Separation from Service, then, solely to the extent necessary to avoid the imposition of the adverse personal tax consequences under Section 409A of the Code, (A) the commencement of such benefit payments will be delayed until the earlier of (1) the date that is six (6) months and one (1) day after such Separation from Service and (2) the date of the Employee's death (such applicable date, the "Delayed Initial Payment Date"), and (B) the Company will (1) pay the Employee a lump sum amount equal to the sum of any benefit payments that the Employee otherwise would have received through the Delayed Initial Payment Date if the commencement of such benefit payments had not been delayed pursuant to this paragraph and (2) commence paying the balance, if any, of such benefit in accordance with the applicable payment schedule.

It is intended that each installment of any benefit payable under this Agreement be regarded as a separate "payment" for purposes of Treasury Regulations Section 1.409A-2(b)(2)(i).

5. Limitation on Payments. In the event that the severance and other benefits provided for in this Agreement or otherwise payable to the Employee (i) constitute "parachute payments" within the meaning of Section 280G of the Code, and (ii) would be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then Employee's benefits under this Agreement shall be either

(a) delivered in full, or

(b) delivered as to such lesser extent which would result in no portion of such benefits being subject to the Excise Tax,

whichever of the foregoing amounts, taking into account the applicable federal, state and local income taxes and the Excise Tax, results in the receipt by Employee on an after-tax basis, of the greatest amount of benefits, notwithstanding that all or some portion of such benefits may be taxable under Section 4999 of the Code.

Unless the Company and the Employee otherwise agree in writing, any determination required under this Section shall be made in writing by the Company's independent public accountants (the "Accountants"), whose determination shall be conclusive and binding upon the Employee and the Company for all purposes. For purposes of making the calculations required by this Section, the Accountants may make reasonable assumptions and approximations concerning applicable taxes and may rely on reasonable, good faith interpretations concerning the application of Section 280G and 4999 of the Code. The Company and the Employee shall furnish to the Accountants such information and documents as the Accountants may reasonably request in order to make a determination under this Section. The Company shall bear all costs the Accountants may reasonably incur in connection with any calculations contemplated by this Section.

6. Successors.

(a) Company's Successors. Any successor to the Company (whether direct or indirect and whether by purchase, lease, merger, consolidation, liquidation or otherwise) to all or substantially all of the Company's business and/or assets shall assume the Company's obligations under this Agreement and agree expressly to perform the Company's obligations under this Agreement in the same manner and to the same extent as the Company would be required to perform such obligations in the absence of a succession. For all purposes under this Agreement, the term "Company" shall include any successor to the Company's business and/or assets which executes and delivers the assumption agreement described in this subsection (a) or which becomes bound by the terms of this Agreement by operation of law.

(b) Employee's Successors. Without the written consent of the Company, Employee shall not assign or transfer this Agreement or any right or obligation under this Agreement to any other person or entity. Notwithstanding the foregoing, the terms of this

Agreement and all rights of Employee hereunder shall inure to the benefit of, and be enforceable by, Employee's personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees.

7. Execution of Release Agreement upon Termination. As a condition of entering into this Agreement and receiving the benefits under Section 4(a), the Employee agrees to execute and not revoke a general release of claims within forty-five (45) days following the termination of employment with the Company.

8. Notices.

(a) General. Notices and all other communications contemplated by this Agreement shall be in writing and shall be deemed to have been duly given when personally delivered or when mailed by U.S. registered or certified mail, return receipt requested and postage prepaid. In the case of the Employee, mailed notices shall be addressed to Employee at the home address which Employee most recently communicated to the Company in writing. In the case of the Company, mailed notices shall be addressed to its corporate headquarters, and all notices shall be directed to the attention of its Chief Executive Officer.

(b) Notice of Termination. Any termination by the Company for Cause or by the Employee as a result of a voluntary resignation or an Involuntary Resignation shall be communicated by a notice of termination to the other party hereto given in accordance with this Section. Such notice shall indicate the specific termination provision in this Agreement relied upon, shall set forth in reasonable detail the facts and circumstances claimed to provide a basis for termination under the provision so indicated, and shall specify the Termination Date (which shall be not more than 30 days after the giving of such notice, such period to be extended to the extent a 30 day cure period under Section 1(c) applies). Except for the notice required under Section 1(c), the failure by the Employee to provide notice under this Section 8(b) shall not waive any right of the Employee hereunder or preclude the Employee from asserting any fact or circumstance in enforcing his rights hereunder.

9. Arbitration.

(a) Any dispute or controversy arising out of, relating to, or in connection with this Agreement, or the interpretation, validity, construction, performance, breach, or termination thereof, shall be settled by binding arbitration to be held in Santa Clara, California, in accordance with the National Rules for the Resolution of Employment Disputes then in effect of the American Arbitration Association (the "Rules"). The arbitrator may grant injunctions or other relief in such dispute or controversy. The decision of the arbitrator shall be final, conclusive and binding on the parties to the arbitration. Judgment may be entered on the arbitrator's decision in any court having jurisdiction. The arbitrator may require one party to pay the costs and attorney fees of the prevailing party.

(b) The arbitrator(s) shall apply California law to the merits of any dispute or claim, without reference to conflicts of law rules. The arbitration proceedings shall be governed by federal arbitration law and by the Rules, without reference to state arbitration law. Employee hereby consents to the personal jurisdiction of the state and federal courts located in California

for any action or proceeding arising from or relating to this Agreement or relating to any arbitration in which the parties are participants.

(c) Employee understands that nothing in this Section modifies Employee's at-will employment status. Either Employee or the Company can terminate the employment relationship at any time, with or without Cause.

(d) EMPLOYEE HAS READ AND UNDERSTANDS THIS SECTION, WHICH DISCUSSES ARBITRATION. EMPLOYEE UNDERSTANDS THAT SUBMITTING ANY CLAIMS ARISING OUT OF, RELATING TO, OR IN CONNECTION WITH THIS AGREEMENT, OR THE INTERPRETATION, VALIDITY, CONSTRUCTION, PERFORMANCE, BREACH OR TERMINATION THEREOF TO BINDING ARBITRATION, CONSTITUTES A WAIVER OF EMPLOYEE'S RIGHT TO A JURY TRIAL AND RELATES TO THE RESOLUTION OF ALL DISPUTES RELATING TO ALL ASPECTS OF THE EMPLOYER/EMPLOYEE RELATIONSHIP, INCLUDING BUT NOT LIMITED TO, THE FOLLOWING CLAIMS:

(i) ANY AND ALL CLAIMS FOR WRONGFUL DISCHARGE OF EMPLOYMENT; BREACH OF CONTRACT, BOTH EXPRESS AND IMPLIED; BREACH OF THE COVENANT OF GOOD FAITH AND FAIR DEALING, BOTH EXPRESS AND IMPLIED; NEGLIGENT OR INTENTIONAL INFLICTION OF EMOTIONAL DISTRESS; NEGLIGENT OR INTENTIONAL MISREPRESENTATION; NEGLIGENT OR INTENTIONAL INTERFERENCE WITH CONTRACT OR PROSPECTIVE ECONOMIC ADVANTAGE; AND DEFAMATION.

(ii) ANY AND ALL CLAIMS FOR VIOLATION OF ANY FEDERAL STATE OR MUNICIPAL STATUTE, INCLUDING, BUT NOT LIMITED TO, TITLE VII OF THE CIVIL RIGHTS ACT OF 1964, THE CIVIL RIGHTS ACT OF 1991, 1 AGE DISCRIMINATION IN EMPLOYMENT ACT OF 1967, THE AMERICANS WITH DISABILITIES ACT OF 1990, THE FAIR LABOR STANDARDS ACT, THE CALIFORNIA FAIR EMPLOYMENT AND HOUSING ACT, AND LABOR CODE SECTION 20 1, *et seq*;

(iii) ANY AND ALL CLAIMS ARISING OUT OF ANY OTHER LAWS AND REGULATIONS RELATING TO EMPLOYMENT OR EMPLOYMENT DISCRIMINATION.

10. Miscellaneous Provisions.

(a) Effect of Statutory Benefits. To the extent that any severance benefits are required to be paid to the Employee upon termination of employment with the Company as a result of any requirement of law or any governmental entity in any applicable jurisdiction, the aggregate amount of severance benefits payable pursuant to Section 4 hereof shall be reduced by such amount.

(b) No Duty to Mitigate. The Employee shall not be required to mitigate the amount of any payment contemplated by this Agreement, nor shall any such payment be reduced by any earnings that the Employee may receive from any other source.

(c) Waiver. No provision of this Agreement may be modified, waived or discharged unless the modification, waiver or discharge is agreed to in writing and signed by the Employee and by an authorized officer of the Company (other than the Employee). No waiver by either party of any breach of, or of compliance with, any condition or provision of this Agreement by the other party shall be considered a waiver of any other condition or provision or of the same condition or provision at another time.

(d) Integration. This Agreement and any outstanding stock option agreements and any restricted stock purchase agreements referenced herein represent the entire agreement and understanding between the parties as to the subject matter herein and supersede all prior or contemporaneous agreements, whether written or oral , with respect to this Agreement and any stock option agreement or any restricted stock purchase agreement, provided, that, for clarification purposes, this Agreement shall not affect any agreements between the Company and Employee regarding intellectual property matters or confidential information of the Company.

(e) Choice of Law. The validity, interpretation, construction and performance of this Agreement shall be governed by the internal substantive laws, but not the conflicts of law rules, of the State of California.

(f) Severability. The invalidity or unenforceability of any provision or provisions of this Agreement shall not affect the validity or enforceability of any other provision hereof, which shall remain in full force and effect.

(g) Employment Taxes. All payments made pursuant to this Agreement shall be subject to withholding of applicable income and employment taxes.

(h) Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together will constitute one and the same instrument.

IN WITNESS WHEREOF, each of the parties has executed this Agreement, in the case of the Company by its duly authorized officer, as of the day and year first above written.

COMPANY: Threshold Pharmaceuticals, Inc.

By: _____

Title: _____

EMPLOYEE:

_____
Signature

_____
Printed Name

Exhibit 12.1

Computation of Ratio of Earnings to Fixed Charges and Ratio of Earnings to Combined Fixed Charges and Preferred Stock Dividends

	Year Ended December 31,				
	2010	**2011**	**2012**	**2013**	**2014**
Earnings:					
Loss before income taxes	$ (18,682)	$ (25,653)	$ (71,135)	$ (28,213)	$ (21,786)
Add Fixed Charges (from below)	374	329	225	187	250
Total earnings (loss) to cover fixed charges	(18,308)	(25,324)	(70,910)	(28,026)	(21,536)
Fixed Charges:					
Interest expense	—	—	—	—	—
Interest component of rent expense[1]	374	329	225	187	250
Total fixed charges	374	329	225	187	250
Ratio of earnings to fixed charges[2]	N/A[3]	N/A[3]	N/A[3]	N/A[3]	N/A[3]

(1) Represents the estimated portion of rental expense from operating leases that is considered by us to be representative of interest.

(2) We have not had any preferred stock outstanding during the periods presented; therefore, the ratio of earnings to (and the deficiency of earnings available to cover) combined fixed charges and preferred stock dividends is the same as our ratio of earnings to (and the deficiency of earnings available to cover) fixed charges alone.

(3) Earnings were insufficient to cover fixed charges for each of the periods presented. The amount of the coverage deficiency was $18.7 million, $25.7 million, $71.1 million, $28.2 million and $21.8 million for the years ended December 31, 2010, 2011, 2012, 2013 and 2014, respectively.

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. 333-195084, No. 333-174844, No. 333-169689, 333-162719 and 333-153475) and Registration Statements on Form S-8 (No. 333-196249, 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 2014 Equity Incentive Plan, the Amended and Restated 2004 Equity Incentive Plan, the 2004 Equity Incentive Plan, the Amended and Restated 2004 Employee Stock Purchase Plan and the 2004 Employee Stock Purchase Plan of Threshold Pharmaceuticals, Inc. of our reports dated March 3, 2015, 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, 2014.

/s/ Ernst & Young LLP

San Jose, California
March 3, 2015

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 3, 2015

/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 3, 2015

/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, 2014, 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 3, 2015

/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, 2014, 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 3, 2015

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