

Prospectus



## 25,654,418 Shares of Common Stock

This prospectus relates to the sale from time to time by the selling stockholders identified in this prospectus for their own account of up to a total of 25,654,418 shares of our common stock, including up to an aggregate of 7,329,819 shares of our common stock issuable upon the exercise of warrants. The selling stockholders acquired their shares in a private placement of shares of common stock and warrants to purchase shares of common stock completed on October 5, 2009.

We will not receive any of the proceeds from the sale of shares by the selling stockholders. However, we will receive the proceeds from the exercise of the warrants by the selling stockholders, if any, to the extent that the warrants are not exercised on a cashless basis. See "[Use of Proceeds](#)" beginning on page 18 of this prospectus.

Our common stock trades on the NASDAQ Capital Market under the symbol "THLD." The last reported sales price per share of our common stock as reported by the NASDAQ Capital Market on November 11, 2009 was \$1.94.

The selling stockholders may, from time to time, offer and sell or otherwise dispose of any or all of the shares of common stock described in this prospectus on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices, and may be to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions. The selling stockholders will bear all discounts, concessions, commissions and similar expenses, if any, attributable to the sale of shares. We will bear all other costs, expenses, and fees in connection with the registration of the shares. See "[Plan of Distribution](#)" beginning on page 28 for more information about how the selling stockholders may sell or dispose of their shares of common stock.

**INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. BEFORE BUYING ANY SHARES, YOU SHOULD CAREFULLY READ THE DISCUSSION OF MATERIAL RISKS OF INVESTING IN OUR COMMON STOCK IN "[RISK FACTORS](#)" BEGINNING ON PAGE 4 OF THIS PROSPECTUS.**

**NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.**

**The date of this prospectus is November 12, 2009.**

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### **About this Prospectus**

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information contained in this prospectus is accurate only as of the date of this prospectus, and that information contained in any document included in this prospectus is accurate only as of the date of that document, regardless of the time of delivery of this prospectus or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since such dates.

Market data and certain industry forecasts used in this prospectus and the documents included in this prospectus were obtained from market research, publicly available information and industry publications. We believe that these sources are generally reliable, but the accuracy and completeness of such information is not guaranteed. We have not independently verified this information, and we do not make any representation as to the accuracy of such information.

In this prospectus, unless the context otherwise requires, references to “we,” “us,” “our” or similar terms, as well as references to “Threshold Pharmaceuticals” or the “Company,” refer to Threshold Pharmaceuticals, Inc., either alone or together with our subsidiaries.

The name Threshold Pharmaceuticals, Inc. is our trademark. Other trademarks, product names and company names appearing in this prospectus and documents included in this prospectus or incorporated by reference in this prospectus are the property of their respective owners.

**PROSPECTUS SUMMARY**

*This summary highlights key aspects of the information contained elsewhere in this prospectus. This summary does not contain all the information you should consider before investing in our securities. You should read this entire prospectus carefully, especially the risks of investing in our securities discussed under "[Risk Factors](#)" beginning on page 4 of this prospectus before making an investment decision.*

**Company Information**

We are a biotechnology company focused on the discovery and development of drugs targeting the microenvironment of solid tumors as novel treatments for patients living with cancer. The microenvironment of solid tumors is characterized by, among other things, hypoxia or lack of oxygen, disordered blood vessel growth, and the upregulation of glucose transport. This hypoxic environment is known to be resistant to standard chemotherapy and radiation. It is thought to be responsible for the poor prognosis of many solid tumors and treating the hypoxic environment is currently believed to be a significant unmet medical need. Our product candidates are designed to selectively target the hypoxic microenvironment of tumors either by selective toxin activation in the case of our hypoxia activated prodrug (HAP) program, including TH-302, or potentially utilizing the consequences of increased uptake of glucose in cancer cells relative to most normal cells. Our product candidate 2DG shares certain structural characteristics with glucose but acts instead as a chemotherapeutic toxin when taken up by a cell.

We were incorporated in Delaware on October 17, 2001. Our principal executive offices are located at 1300 Seaport Boulevard, Suite 500 Redwood City, California, 94063. Our telephone number is (650) 474-8200. Our website is located at <http://www.thresholdpharm.com>. Information contained on, or that can be accessed through, our website is not part of this prospectus.

**THE OFFERING**

<b>Securities Offered</b>	Up to 25,654,418 shares of our common by certain selling stockholders, of which 7,329,819 are issuable upon the exercise of warrants.
<b>Manner of Offering</b>	The selling stockholders, either directly or through broker-dealers or agents, may offer and sell their securities on a continuous or delayed basis in the future. These sales may be conducted in the open market or in privately negotiated transactions and at prevailing market prices, fixed prices or negotiated prices. See " <a href="#">Plan of Distribution</a> " beginning on page 28 of this prospectus.
<b>Use of Proceeds</b>	We will not receive any proceeds from the sale of the shares by the selling stockholders. Nevertheless, we may receive proceeds from the exercise of the warrants, if any, to the extent the warrants are not exercised on a cashless basis. See " <a href="#">Use of Proceeds</a> " beginning on page 18 of this prospectus.
<b>Trading Symbol for our Common Stock</b>	Our common stock is traded on the NASDAQ Capital Market under the symbol "THLD."

Unless specifically stated otherwise, the information in this prospectus assumes no exercise of outstanding options or warrants.

## RISK FACTORS

*Investing in our securities involves a high degree of risk. You should carefully consider the specific risks described below, together with all other information contained in this prospectus, the risks described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2008, our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2009, June 30, 2009 and September 30, 2009, and any risks described in our other filings with the SEC pursuant to Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, before deciding to invest in our common stock. See the section of this prospectus entitled "Where You Can Find Additional Information." Any of the risks we describe below or in the information incorporated herein by reference could cause our business, financial condition or results of operations to suffer. The market price of our common stock could decline if one or more of these risks and uncertainties develop into actual events. You could lose all or part of your investment. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, or operating results. Some of the statements in this section of the prospectus are forward-looking statements. For more information about forward-looking statements, please see the section of this prospectus entitled "Cautionary Note Regarding Forward-Looking Statements."*

### Risks Related to Drug Discovery, Development and Commercialization

***We are substantially dependent upon the success of TH-302 and our other product candidates. Clinical trials may not demonstrate efficacy or lead to regulatory approval and preliminary results may not be confirmed.***

We will not be able to commercialize our drug candidates until we obtain FDA approval in the United States or approval by comparable regulatory agencies in Europe and other countries. To satisfy FDA or foreign regulatory approval standards for the commercial sale of our product candidates, we must demonstrate in adequate and controlled clinical trials that our product candidates are safe and effective. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Our preliminary results from clinical trials of TH-302 in a small number of patients may not be confirmed by later analysis or subsequent larger clinical trials. A number of companies in the pharmaceutical industry, including us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

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

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

We cannot be certain of successfully completing clinical testing within the time frame we have planned, or at all. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our product candidates, including the following:

- our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and/or preclinical testing or to abandon programs;
- the results obtained in earlier stage clinical testing may not be indicative of results in future clinical trials;
- clinical trial results may not meet the level of statistical significance required by the FDA or other regulatory agencies;
- enrollment in our clinical trials for our product candidates may be slower than we anticipate, resulting in significant delays;
- we, or regulators, may suspend or terminate our clinical trials if the participating patients are being exposed to unacceptable health risks; and
- the effects of our product candidates on patients may not be the desired effects or may include undesirable side effects or other characteristics that may delay or preclude regulatory approval or limit their commercial use, if approved.

Completion of clinical trials depends, among other things, on our ability to enroll a sufficient number of patients, which is a function of many factors, including:

- the therapeutic endpoints chosen for evaluation;
- the eligibility criteria defined in the protocol;
- the 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;

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- our ability to obtain and maintain patient consents; and
- competition for patients by clinical trial programs for other treatments.

We may experience difficulties in enrolling patients in our clinical trials, which could increase the costs or affect the timing or outcome of these clinical trials. This is particularly true with respect to diseases with relatively small patient populations.

### ***Pre-clinical studies of our product candidates may not predict the results of their human clinical trials.***

Pre-clinical studies, including studies of our product candidates in animal models of disease, may not accurately predict the result of human clinical trials of those product candidates. In particular, promising animal studies suggesting the efficacy of TH-302 for the treatment of different types of cancer may not accurately predict the ability of TH-302 to treat cancer effectively in humans. TH-302 may be found not to be efficacious in treating cancer, alone or in combination with other agents, when studied in human clinical trials.

### ***We are subject to significant regulatory approval requirements, which could delay, prevent or limit our ability to market our product candidates.***

Our research and development activities, preclinical studies, clinical trials and the anticipated manufacturing and marketing of our product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in Europe and elsewhere. We require the approval of the relevant regulatory authorities before we may commence commercial sales of our product candidates in a given market. The regulatory approval process is expensive and time-consuming, and the timing of receipt of regulatory approval is difficult to predict. Our product candidates could require a significantly longer time to gain regulatory approval than expected, or may never gain approval. We cannot be certain that, even after expending substantial time and financial resources, we will obtain regulatory approval for any of our product candidates. A delay or denial of regulatory approval could delay or prevent our ability to generate product revenues and to achieve profitability.

Changes in regulatory approval policies during the development period of any of our product candidates, changes in, or the enactment of, additional regulations or statutes, or changes in regulatory review practices for a submitted product application may cause a delay in obtaining approval or result in the rejection of an application for regulatory approval.

Regulatory approval, if obtained, may be made subject to limitations on the indicated uses for which we may market a product. These limitations could adversely affect our potential product revenues. Regulatory approval may also require costly post-marketing follow-up studies. In addition, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping related to the product will be subject to extensive ongoing regulatory requirements. Furthermore, for any marketed product, its manufacturer and its manufacturing facilities will be subject to continual review and periodic inspections by the FDA or other regulatory authorities. Failure to comply with applicable regulatory requirements may, among other things, result in fines, suspensions of regulatory approvals, product recalls, product seizures, operating restrictions and criminal prosecution.

### ***Our product candidates are based on targeting the microenvironment of solid tumors, which currently are unproven approaches to therapeutic intervention.***

Our product candidates are designed to target the microenvironment of solid tumors either by harnessing hypoxia for selective toxin activation in the case of TH-302 and our HAP program or potentially utilizing the increased uptake of glucose in cancer cells relative to most normal cells. Our product candidate 2DG shares certain structural characteristics with glucose but acts instead as a poison when taken up by a cancer cell. We have not, nor to our knowledge has any other company, received regulatory approval for a drug based on either of these approaches. We cannot be certain that our approaches will lead to the development of approvable or marketable drugs.

In addition, the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of drugs based on these targeting approaches, which could lengthen the regulatory review process, increase our development costs and delay or prevent commercialization of our product candidates.

### ***Our product candidates may have undesirable side effects that prevent or delay their regulatory approval or limit their use if approved.***

Certain anti-tumor drugs being developed by us, such as TH-302 and 2DG, are expected to have undesirable side effects. The extent, severity and clinical significance of these effects may not be apparent initially and may be discovered during drug development or even post-approval. These expected side effects or other side effects identified in the course of our clinical trials or that may otherwise be associated with our product candidates may outweigh the benefits of our product candidates. Side effects may prevent or delay regulatory approval or limit market acceptance if our products are approved.

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### ***Delays in clinical testing could result in increased costs to us and delay our ability to obtain regulatory approval and commercialize our product candidates.***

Significant delays in clinical testing could materially impact our product development costs and delay regulatory approval of our product candidates. We do not know whether planned clinical trials will need to be redesigned or 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 and delays in:

- obtaining regulatory approval to commence a clinical trial;
- obtaining clinical materials;
- reaching agreement on acceptable clinical trial agreement terms with prospective sites;
- obtaining institutional review board approval to conduct a clinical trial at a prospective site; and
- recruiting patients to participate in a clinical trial.

### ***Orphan drug exclusivity affords us limited protection, and if another party obtains orphan drug exclusivity for the drugs and indications we are targeting, we may be precluded from commercializing our product candidates in those indications.***

For those drugs that meet the eligible requirements, we intend to seek orphan drug designation for the cancer indications that our drug candidates are intended to treat. Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is defined by the FDA as a disease or condition that affects fewer than 200,000 individuals in the United States. The company that obtains the first FDA approval for a designated orphan drug indication receives marketing exclusivity for use of that drug for that indication for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug. Orphan drug designation does not shorten the development or regulatory review time of a drug.

Orphan drug exclusivity may not prevent other market entrants. A different drug, or, under limited circumstances, the same drug may be approved by the FDA for the same orphan indication. The limited circumstances include an inability to supply the drug in sufficient quantities or where a new formulation of the drug has shown superior safety or efficacy. As a result, if our product is approved and receives orphan drug status, the FDA can still approve other drugs for use in treating the same indication covered by our product, which could create a more competitive market for us.

Moreover, due to the uncertainties associated with developing pharmaceutical products, we may not be the first to obtain marketing approval for any orphan drug indication. Even if we obtain orphan drug designation, if a competitor obtains regulatory approval for TH-302 or 2DG for the same indication we are targeting before we do, we would be blocked from obtaining approval for that indication for seven years, unless our product is a new formulation of the drug that has shown superior safety or efficacy, or the competitor is unable to supply sufficient quantities.

### ***Even if we obtain regulatory approval, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing United States and foreign regulations, we could lose our approvals to market drugs and our business would be seriously harmed.***

Following initial regulatory approval of any drugs we may develop, we will be subject to continuing regulatory review, including review of adverse drug experiences and clinical results that are reported after our drug products become commercially available. This would include results from any post-marketing tests or vigilance required as a condition of approval. The manufacturer and manufacturing facilities we use to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. If a previously unknown problem or problems with a product or a manufacturing and laboratory facility used by us is discovered, the FDA or foreign regulatory agency may impose restrictions on that product or on the manufacturing facility, including requiring us to withdraw the product from the market. Any changes to an approved product, including the way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our contract manufacturers will be subject to ongoing FDA requirements for submission of safety and other post-market information. If we and our contract manufacturers fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw our regulatory approval;
- suspend or terminate any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on our operations;
- close the facilities of our contract manufacturers; or
- seize or detain products or require a product recall.



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

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

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

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

### **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 are a development stage company with a limited operating history and no current source of revenue from the sale of our product candidates. We have incurred losses in each year since our inception in 2001, 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 nine months ended September 30, 2009, we had a net loss of \$18.9 million and our cumulative net loss since our inception through September 30, 2009 was \$203.1 million. Clinical trials are costly. We do not expect to generate any revenue from the sale of our product candidates in the near term, and we expect to continue to have significant losses for the foreseeable future.

To attain profitability, we will need to develop products successfully and market and sell them effectively. We cannot predict when we will become profitable, if at all. We have never generated revenue from the sale 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.

#### ***We are likely to require substantial additional funding and may be unable to raise capital when needed, which could force us to delay, reduce or eliminate our drug discovery, product development and commercialization activities.***

Developing drugs, conducting clinical trials, and commercializing products is expensive. Our future funding requirements will depend on many factors, including:

- the terms and timing of any collaborative, licensing, acquisition or other arrangements that we may establish;

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- the progress and cost of our clinical trials and other research and development activities;
- the costs and timing of obtaining regulatory approvals;
- the costs of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights;
- the cost and timing of securing manufacturing capabilities for our clinical product candidates and commercial products, if any; and
- the costs of lawsuits involving us or our product candidates.

We believe that our existing cash, cash equivalents and marketable securities as of September 30, 2009 along with the net proceeds from our private placement of shares of common stock and warrants to purchase shares of common stock completed on October 5, 2009, or the 2009 private placement, will be sufficient to fund our projected operating requirements through the second quarter of 2011, including prosecuting our current clinical trials, conducting research and discovery efforts towards additional product candidates, working capital and general corporate purposes. Additional funds will be required to in-license or otherwise acquire and develop additional products or programs. We expect to seek funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. We cannot be certain that we will be able to enter into any such arrangements on reasonable terms, if at all.

We expect to need to raise additional capital or incur indebtedness to continue to fund our future operations. We may seek to raise capital through a variety of sources, including:

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

Our ability to raise additional funds will depend, in part on our clinical and regulatory events, our ability to identify promising in-licensing opportunities, and factors related to financial, economic, and market conditions, many of which are beyond our control. We cannot be certain that sufficient funds will be available to us when required or on satisfactory terms, 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 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.

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, President and Chief Medical Officer, Dr. John M. Curd and Senior Vice President of Discovery Research, Dr. Mark G. Matteucci. We do not have employment agreements with Drs. Selick, Curd or Matteucci. The loss of the services of Drs. Selick, Curd 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 September 30, 2009, we had 30 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.

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### ***The reduction in our work force may cause difficulties in conducting operations and maintaining an effective work environment.***

The reductions in our work force in August 2006 and October 2007 imposed significant added responsibilities on remaining management and other employees, including the need to consolidate job functions and to conduct operation with fewer employees. This required that we increase our use of various third parties in order to continue and conduct some operations. Our ability to manage our operations and outside relationships will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. If we are unable to do this effectively, it may be difficult for us to execute our business strategy.

### ***Our facilities in California are located near an earthquake fault, and an earthquake or other natural disaster or resource shortage could disrupt our operations.***

Important documents and records, such as hard copies of our laboratory books and records for our product candidates, are located in our corporate headquarters at a single location in Redwood City, California, near active earthquake zones. In the event of a natural disaster, such as an earthquake, drought or flood, or localized extended outages of critical utilities or transportation systems, we do not have a formal business continuity or disaster recovery plan, and could therefore experience a significant business interruption. In addition, California from time to time has experienced shortages of water, electric power and natural gas. Future shortages and conservation measures could disrupt our operations and could result in additional expense. Although we maintain business interruption insurance coverage, the policy specifically excludes coverage for earthquake and flood.

## **Risks Related to Our Dependence on Third Parties**

### ***We rely on third parties to manufacture TH-302 and 2DG. If these parties do not manufacture the active pharmaceutical ingredients or finished drug products of satisfactory quality, in a timely manner, in sufficient quantities or at an acceptable cost, clinical development and commercialization of our product candidates could be delayed.***

We do not currently own or operate manufacturing facilities; consequently, we rely and expect to continue to rely on third parties for the production of clinical and commercial quantities of our product candidates. We have not yet entered into any long term manufacturing or supply agreement for any of our product candidates. Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our ability to develop and commercialize any product candidates on a timely and competitive basis.

Our contract manufacturers have produced sufficient TH-302 Active Pharmaceutical Ingredient, API, and drug product to meet the clinical supply demands of our ongoing clinical trials. Additional clinical trial material continues to be manufactured as required. We will need to obtain additional supplies of TH-302 API and drug product to complete our Phase 1/2 clinical trials and any other additional trials. The need for additional supplies may require manufacturing process improvements in TH-302 API and drug product. If we are not successful in procuring sufficient TH-302 clinical trial material, we may experience a significant delay in our TH-302 clinical program.

We rely on contract manufacturers for the manufacturing of 2DG API and drug product. If we seek a partner to continue development of 2DG, we will be dependent on contract manufacturers to produce additional API and drug product. If we are not successful, we may experience problems in seeking a partner or in meeting our obligations under a potential partnership to continue development of 2DG.

We will need to enter into additional agreements for additional supplies of each of our product candidates to complete clinical development and/or commercialize them. We cannot be certain that we can do so on favorable terms, if at all. The products will need to satisfy all cGMP manufacturing requirements, including passing specifications. Our inability to satisfy these requirements could delay our clinical programs.

If any of our product candidates is approved by the FDA or other regulatory agencies for commercial sale, we will need to have it manufactured in commercial quantities. We may not be able to increase the manufacturing capacity for any of our product candidates in a timely or economic manner successfully or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA and other regulatory agencies must review and approve. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed, or there may be a shortage of supply which could limit our sales.

In addition, if the facility or the equipment in the facility that produces our product candidates is significantly damaged or destroyed, or if the facility is located in another country and trade or commerce with such country is interrupted, we may be unable to replace the manufacturing capacity quickly or inexpensively. The inability to obtain manufacturing agreements, the damage or destruction of a facility on which we rely for manufacturing or any other delays in obtaining supply would delay or prevent us from completing our clinical trials and commercializing our current product candidates.

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***We have no control over our manufacturers' and suppliers' compliance with manufacturing regulations, and their failure to comply could result in an interruption in the supply of our product candidates.***

The facilities used by our contract manufacturers must undergo an inspection by the FDA for compliance with current good manufacturing practice, or cGMP regulations, before the respective product candidates can be approved. In the event these facilities do not receive a satisfactory cGMP inspection for the manufacture of our product candidates, we may need to fund additional modifications to our manufacturing process, conduct additional validation studies, or find alternative manufacturing facilities, any of which would result in significant cost to us as well as a delay of up to several years in obtaining approval for such product candidate. In addition, our contract manufacturers, and any alternative contract manufacturer we may utilize, will be subject to ongoing periodic inspection by the FDA and corresponding state and foreign agencies for compliance with cGMP regulations, similar foreign regulations and other regulatory standards. We do not have control over our contract manufacturers' compliance with these regulations and standards. Any failure by our third-party manufacturers or suppliers to comply with applicable regulations could result in sanctions being imposed on them (including fines, injunctions and civil penalties), failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecution.

***We rely on third parties to conduct some of our clinical trials, and their failure to perform their obligations in a timely or competent manner may delay development and commercialization of our product candidates.***

We may use clinical research organizations to assist in conduct of our clinical trials. There are numerous alternative sources to provide these services. However, we may face delays outside of our control if these parties do not perform their obligations in a timely or competent fashion or if we are forced to change service providers. This risk is heightened for clinical trials conducted outside of the United States, where it may be more difficult to ensure that clinical trials are conducted in compliance with FDA requirements. Any third-party that we hire to conduct clinical trials may also provide services to our competitors, which could compromise the performance of their obligations to us. If we experience significant delays in the progress of our clinical trials and in our plans to file NDAs, the commercial prospects for product candidates could be harmed and our ability to generate product revenue would be delayed or prevented.

***We may rely on strategic collaborators to market and sell our products.***

We have no sales and marketing experience. We may contract with strategic collaborators to sell and market our products, when and if approved. We may not be successful in entering into collaborative arrangements with third parties for the sale and marketing of any products. Any failure to enter into collaborative arrangements on favorable terms could delay or hinder our ability to develop and commercialize our product candidates and could increase our costs of development and commercialization. Dependence on collaborative arrangements will subject us to a number of risks, including:

- we may not be able to control the amount or timing of resources that our collaborators may devote to the product candidates;
- we may be required to relinquish important rights, including intellectual property, marketing and distribution rights;
- we may have lower revenues than if we were to market and distribute such products ourselves;
- should a collaborator fail to commercialize one of our product candidates successfully, we may not receive future milestone payments or royalties;
- a collaborator could separately move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors;
- our collaborators may experience financial difficulties;
- business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement; and
- our collaborators may operate in countries where their operations could be adversely affected by changes in the local regulatory environment or by political unrest.

***We are dependent on Eleison to develop and commercialize glufosfamide***

We are dependent upon Eleison Pharmaceuticals, Inc. ("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 commence clinical development activities with glufosfamide. Even if Eleison is successful at raising initial funding, it may not be successful in developing and commercializing glufosfamide. 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.

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### Risks Related to Our Intellectual Property

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

Although we have one issued patent that covers a category of hypoxia-activated prodrugs, including TH-302, we have no issued patents or pending patent applications that would prevent others from taking advantage of Hypoxia Activated Prodrug technology generally to discover and develop new therapies for cancer or other diseases. Consequently, our competitors may seek to discover and develop potential therapeutics that operate by mechanisms of action that are the same or similar to the mechanisms of action of our hypoxia activated prodrug product candidates.

***2DG is a known compound that is not protected by patents on the composition of the molecule.***

2DG is a known compound that is no longer eligible for patent protection on the composition of the molecule. A patent of this nature, known as a compound per se patent, excludes others from making, using or selling the patented compound, regardless of how or for what purpose the compound is formulated or intended to be used. Consequently, this compound and certain of its uses are in the public domain.

We have an issued U.S. patent for the use of orally administered 2DG for the treatment of cancer at certain doses and administration schedules, and we have in-licensed three issued U.S. patents that cover the treatment of certain cancers with 2DG in combination with other specific anti-cancer agents.

Others may develop and market 2DG for the treatment of cancer, however, if they develop treatments using dosing and administration schedules or combination therapies outside the scope of our patents or in contravention of our patent rights.

***Metabolic Targeting by targeting the increased uptake of glucose and the increased reliance on glycolysis as an energy source in cancer cells is not protected by patents, and others may be able to develop competitive drugs using this approach.***

We have not issued patents or pending patent applications that would prevent others from taking advantage of targeting the increased uptake of glucose and the increased reliance of glycolysis as an energy source in solid tumors 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 product candidates.

***We are dependent on patents and proprietary technology, both our own and those licensed from others. If we or our licensors fail to adequately protect this intellectual property or if we otherwise do not have exclusivity for the marketing of our products, our ability to commercialize products could suffer.***

Our commercial success will depend in part on our ability and the ability of our licensors to obtain and maintain patent protection sufficient to prevent others from marketing our product candidates, as well as to 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 if they are effectively protected by trade secrets. If our patent applications do not result in issued patents, or if our patents, or those patents we have licensed, are found to be invalid, we will lose the ability to exclude others from making, using or selling the inventions claimed therein. We have a limited number of patents and pending patent applications.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the United States. The laws of many countries may not protect intellectual property rights to the same extent as United States laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. We do not know whether any of our patent applications will result in the issuance of any patents and we cannot predict the breadth of claims that may be allowed in our patent applications or in the patent applications we license from others.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our or our licensors' pending patent applications and issued patents, and we may have to participate in expensive and protracted interference proceedings to determine priority of invention;
- we or our licensors might not have been the first to file patent applications for these inventions;

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- others may independently develop similar or alternative product candidates or duplicate any of our or our licensors' product candidates;
- our or our licensors' pending patent applications may not result in issued patents;
- our or our licensors' issued patents may not provide a basis for commercially viable products or may not provide us with any competitive advantages or may be challenged by third parties;
- others may design around our or our licensors' patent claims to produce competitive products that fall outside the scope of our or our licensors' patents;
- we may not develop or in-license additional patentable proprietary technologies related to our product candidates; or
- the patents of others may prevent us from marketing one or more of our product candidates for one or more indications that may be valuable to our business strategy.

Moreover, an issued patent does not guarantee us the right to practice the patented technology or commercialize the patented product. Third parties may have blocking patents that could be used to prevent us from commercializing our patented products and practicing our patented technology. Our issued patents and those that may be issued in the future may be challenged, invalidated or circumvented, which could limit our ability to prevent competitors from marketing the same or related product candidates or could limit the length of the term of patent protection of our product candidates. In addition, the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent. Patent term extensions may not be available for these patents.

***We rely on trade secrets and other forms of non-patent intellectual property protection. If we are unable to protect our trade secrets, other companies may be able to compete more effectively against us.***

We rely on trade secrets to protect certain aspects of our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be made public during the regulatory approval process. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secret information is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to or may not protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

***If we are sued for infringing intellectual property rights of third parties or if we are forced to engage in an interference proceeding, it will be costly and time consuming, and an unfavorable outcome in that litigation or interference would have a material adverse effect on our business.***

Our ability to commercialize our product candidates depends on our ability to develop, manufacture, market and sell our product candidates without infringing the proprietary rights of third parties. Numerous United States and foreign issued patents and pending 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. We are also aware of a patent that claims certain agents, including 2DG, to inhibit the import of glucose-6-phosphate into the endoplasmic reticulum of a cell. We do not know whether administration of 2DG for our intended uses inhibits such import. If it does, we would be required to license the patent or risk that a claim of infringement could be made. If we are shown to infringe, we could be enjoined from use or sale of the claimed invention if we are unable to prove that the patent is invalid. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our product candidates or any other compound that we may develop, may infringe, or which may trigger an interference proceeding regarding one of our owned or licensed patents or applications. There could also be existing patents of which we are not aware that our product candidates may inadvertently infringe or which may become involved in an interference proceeding.

The biotechnology and biopharmaceutical industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. For so long as our product candidates are in clinical trials, we believe our clinical activities fall within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the United States, which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. As our clinical investigational drugs progress toward commercialization, the possibility of a patent infringement claim against us increases. While we attempt to ensure that our active clinical investigational drugs and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties' patents and other proprietary rights, we cannot be certain they do not, and competitors or other parties may assert that we infringe their proprietary rights in any event.

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We may be exposed to future litigation based on claims that our product candidates, or the methods we employ to manufacture them, or the uses for which we intend to promote them, infringe the intellectual property rights of others. Our ability to manufacture and commercialize our product candidates may depend on our ability to demonstrate that the manufacturing processes we employ and the use of our product candidates do not infringe third-party patents. If third-party patents were found to cover our product candidates or their use or manufacture, we could be required to pay damages or be enjoined and therefore unable to commercialize our product candidates, unless we obtained a license. A license may not be available to us on acceptable terms, if at all.

### **Risks Related To Our Industry**

*If our competitors are able to develop and market products that are more effective, safer or more affordable than ours, or obtain marketing approval before we do, our commercial opportunities may be limited.*

Competition in the biotechnology and pharmaceutical industries is intense and continues to increase, particularly in the area of cancer treatment. Most major pharmaceutical companies and many biotechnology companies are aggressively pursuing oncology development programs, including traditional therapies and therapies with novel mechanisms of action. Our cancer product candidates face competition from established biotechnology and pharmaceutical companies, including sanofi-aventis, AstraZeneca PLC, Genentech, Inc., Bayer Corporation, Eli Lilly and Company and Pfizer, Inc., and from generic pharmaceutical manufacturers. In particular, our drug candidates for pancreatic cancer will compete with Gemzar, marketed by Eli Lilly and Company, doxorubicin, cisplatin, paclitaxel, ifosfamide, and 5-fluorouracil, or 5-FU, a generic product which is sold by many manufacturers. In addition, several drugs marketed for different indications, such as Camptosar®, marketed by Pfizer, Inc., Erbitux®, marketed by Imclone Systems Inc. and Bristol-Myers Squibb Company, Taxotere®, marketed by sanofi-aventis, DTIC-Dome®, marketed by Bayer Pharmaceuticals Corporation, Xeloda®, marketed by Hoffmann-LaRoche, Inc., Avastin®, marketed by Genentech, Inc., Nexavar®, marketed by Onyx Pharmaceuticals, Inc. and Bayer AG, and Alimta®, marketed by Eli Lilly and Company, are under investigation or have completed investigation as combination therapies or monotherapy for pancreatic, prostate, ovarian, non small cell lung and small cell lung cancers, melanoma and soft tissue sarcoma. Additionally, OSI Pharmaceuticals, Inc. and Genentech, Inc. market Tarceva® as a combination therapy with gemcitabine for the first-line treatment of pancreatic cancer. In addition, Proacta Inc. has a compound under clinical investigation that targets the hypoxic zones of tumors, as our TH-302 clinical product candidate is intended to do. Novacea has conducted studies on AQ4N and sanofi-aventis recently completed a Phase 3 clinical trial on Tirapazamine, a hypoxically activated prodrug, and while Novacea has stopped current clinical development of AQ4N and sanofi-aventis has released rights to the compound to the innovator SRI, another company may pursue further clinical development of either compound.

We also face potential competition from academic institutions, government agencies and private and public research institutions engaged in the discovery and development of drugs and therapies. Many of our competitors have significantly greater financial resources and expertise in research and development, preclinical testing, conducting clinical trials, obtaining regulatory approvals, manufacturing, sales and marketing than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established pharmaceutical companies.

Our competitors may succeed in developing products that are more effective, have fewer side effects and are safer or more affordable than our product candidates, which would render our product candidates less competitive or noncompetitive. These competitors also compete with us to recruit and retain qualified scientific and management personnel, establish clinical trial sites and patient registration for clinical trials, as well as to acquire technologies and technology licenses complementary to our programs or advantageous to our business. Moreover, competitors that are able to achieve patent protection obtain regulatory approvals and commence commercial sales of their products before we do, and competitors that have already done so, may enjoy a significant competitive advantage.

*There is a substantial risk of product liability claims in our business. If we do not obtain sufficient liability insurance, a product liability claim could result in substantial liabilities.*

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and marketing of human therapeutic products. Regardless of merit or eventual outcome, product liability claims may result in:

- delay or failure to complete our clinical trials;
- withdrawal of clinical trial participants;
- decreased demand for our product candidates;
- injury to our reputation;
- litigation costs;
- substantial monetary awards against us; and



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- 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 an \$8 million annual aggregate limit. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for our product candidates or any other compound that we may develop. However, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or at all, and the insurance coverage that we obtain may not be adequate to cover potential claims or losses.

***Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which would negatively affect our ability to achieve profitability.***

Our product candidates may not gain market acceptance among physicians, patients, healthcare payors and the medical community. The degree of market acceptance of any approved products will depend on a number of factors, including:

- the effectiveness of the product;
- the prevalence and severity of any side effects;
- potential advantages or disadvantages over alternative treatments;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the price of the product, both in absolute terms and relative to alternative treatments; and
- sufficient third-party coverage or reimbursement.

If our product candidates receive regulatory approval but do not achieve an adequate level of acceptance by physicians, healthcare payors and patients, we may not generate product revenues sufficient to attain profitability.

***If third-party payors do not adequately reimburse patients for any of our product candidates, if approved for marketing, we may not be successful in selling them.***

Our ability to commercialize any products successfully will depend in part on the extent to which reimbursement will be available from governmental and other third-party payors, both in the United States and in foreign markets. Even if we succeed in bringing one or more products to the market, the amount reimbursed for our products may be insufficient to allow us to compete effectively and could adversely affect our profitability.

Reimbursement by a governmental and other third-party payor may depend upon a number of factors, including a governmental or other third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining reimbursement approval for a product from each third-party and governmental payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor. We may not be able to provide data sufficient to obtain reimbursement.

Eligibility for coverage does not imply that any drug product will be reimbursed in all cases or at a rate that allows us to make a profit. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not become permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or Medicare or Medicaid data used to calculate these rates. Net prices for products also may be reduced by mandatory discounts or rebates required by government health care programs or by any future relaxation of laws that restrict imports of certain medical products from countries where they may be sold at lower prices than in the United States.



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The health care industry is experiencing a trend toward containing or reducing costs through various means, including lowering reimbursement rates, limiting therapeutic class coverage and negotiating reduced payment schedules with service providers for drug products. The Medicare Prescription Drug, Improvement and Modernization Act of 2003, or MMA, became law in November 2003 and created a broader prescription drug benefit for Medicare beneficiaries. The MMA also contains provisions intended to reduce or eliminate delays in the introduction of generic drug competition at the end of patent or nonpatent market exclusivity. The impact of the MMA on drug prices and new drug utilization over the next several years is unknown. The MMA also made adjustments to the physician fee schedule and the measure by which prescription drugs are presently paid, changing from Average Wholesale Price to Average Sales Price. The effects of these changes are unknown but may include decreased utilization of new medicines in physician prescribing patterns, and further pressure on drug company sponsors to provide discount programs and reimbursement support programs. There have been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services, which may affect reimbursement levels for our future products. In addition, the Centers for Medicare & Medicaid Services frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates and may have sufficient market power to demand significant price reductions.

### ***Foreign governments tend to impose strict price controls, which may adversely affect our future profitability.***

In some foreign countries, particularly in the European Union, prescription drug pricing is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our profitability will be negatively affected.

### ***We may incur significant costs complying with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.***

Our research and development activities use biological and hazardous materials that are dangerous to human health and safety or the environment. We are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these materials and wastes resulting from these materials. We are also subject to regulation by the Occupational Safety and Health Administration, or OSHA, the California and federal environmental protection agencies and to regulation under the Toxic Substances Control Act. OSHA or the California or federal Environmental Protection Agency, or EPA, may adopt regulations that may affect our research and development programs. We are unable to predict whether any agency will adopt any regulations that could have a material adverse effect on our operations. We have incurred, and will continue to incur, capital and operating expenditures and other costs in the ordinary course of our business in complying with these laws and regulations.

Although we believe our safety procedures for handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot entirely eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of hazardous materials. In the event of contamination or injury, we could be held liable for any resulting damages, and any liability could significantly exceed our insurance coverage.

### ***We may not be able to conduct, or contract with others to conduct, animal testing in the future, which could harm our research and development activities.***

Certain laws and regulations relating to drug development require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

## **Risks Related To Our Common Stock**

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

Our ability to raise additional capital may be dependent upon our stock being quoted on the NASDAQ Capital Market. Previously, we had fallen out of compliance with continued listing requirements because our common stock did not comply with the \$1.00 minimum bid price requirement for continued listing set forth in NASDAQ Marketplace Rule 5450(a)(1) (formerly Rule 4450(a)(5)). To regain compliance, effective August 20, 2008, we implemented a 1-for-6 reverse stock split of our common stock. After that date, our common stock traded above the minimum \$1.00 bid price for at least ten consecutive business days and on September 5, 2008, the NASDAQ Stock Market notified us that we had regained compliance with the minimum bid price requirements. On October 16, 2008, the NASDAQ Stock Market suspended the enforcement of the minimum bid price and market value requirements through January 16, 2009. The suspension period was subsequently extended to July 31, 2009 and NASDAQ's enforcement of these rules resumed on Monday, August 3, 2009. NASDAQ does not expect any further extensions of the suspension. Even though we regained

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compliance with the minimum bid price, we cannot assure you that we will be able to maintain compliance with the minimum bid price requirement or other listing requirements in the future, and our failure to do so could result in the delisting of our shares from the NASDAQ Capital Market.

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

On October 5, 2009, we issued outstanding warrants to purchase an aggregate of 7,329,819 shares of our common stock, at an exercise price of \$2.23 per share. In addition, on August 29, 2008, we issued outstanding warrants to purchase an aggregate of 3,588,221 shares of our common stock, at an exercise price of \$2.34 per share, which exercise price was subsequently reduced to \$1.86 per share on October 5, 2009 under the anti-dilution provisions of the warrants as a result of the 2009 private placement that was completed on that date. The exercise price and/or the number of shares of common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including certain issuances of securities at a price equal to less than the then current exercise price, subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable. Although we cannot determine at this time which of these warrants will ultimately be exercised, it is reasonable to assume that such warrants will be exercised only if the exercise price is below the market price of our common stock. To the extent the warrants are exercised, additional shares of our common stock will be issued that will be eligible for resale in the public market, which will result in dilution to our security holders. The issuance of additional securities could also have an adverse effect on the market price of our common stock.

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

The stock markets in general, the markets for biotechnology stocks and, in particular, the stock price of our common stock, have experienced extreme volatility.

Price declines in our common stock could result from general market and economic conditions and a variety of other factors, including:

- adverse results or delays in our clinical trials;
- announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;
- adverse actions taken by regulatory agencies with respect to our product candidates, clinical trials, manufacturing processes or sales and marketing activities;
- announcements of technological innovations, patents or new products by our competitors;
- regulatory developments in the United States and foreign countries;
- any lawsuit involving us or our product candidates;
- announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;
- developments concerning any strategic alliances or acquisitions we may enter into;
- actual or anticipated variations in our operating results;
- changes in recommendations by securities analysts or lack of analyst coverage;
- deviations in our operating results from the estimates of analysts;

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- sales of our common stock by our executive officers, directors and five percent stockholders or sales of substantial amounts of common stock; and
- loss of any of our key scientific or management personnel.

In the past, following periods of volatility in the market price of a particular company's securities, litigation has often been brought against that company. On July 5 and July 18, 2007, purported shareholder class action complaints alleging violations of the federal securities laws were filed against us, our Chief Executive Officer Harold E. Selick and our former Chief Financial Officer Janet I. Swearson in the United States District Court for the Southern District of New York. On September 14, 2007, these lawsuits, which have been consolidated by the Court into a single proceeding, were ordered transferred to the United States District Court for the Northern District of California. On January 15, 2008, the plaintiffs filed a first consolidated amended complaint. On July 11, 2008, the Court granted the defendants' motions to dismiss that complaint but afforded the plaintiffs leave to file a further amended complaint. On September 19, 2008, the plaintiffs filed a second consolidated amended complaint, which, on behalf of an alleged class of purchasers of our common stock from the date of our initial public offering of securities on February 4, 2005 through July 14, 2006, purports to allege claims arising under Sections 11, 12(a)(2) and 15 of the Securities Act and under Sections 10(b) and 20(a) of the Exchange Act. The plaintiffs allege generally that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning our Phase 2 and Phase 3 clinical trials of Lonidamine (TH-070). On November 14, 2008, Defendants moved to dismiss the second consolidated amended complaint. On April 3, 2009, the Court granted in part and denied in part the motions to dismiss, dismissing with prejudice all claims arising under the Securities Act and all claims against Ms. Swearson, while narrowing the remaining claims. On October 30, 2009, the parties entered into a stipulation of settlement to resolve the lawsuit. The settlement provides for a payment of \$10 million to the plaintiff class solely by our insurers. The settlement is subject to preliminary and, following notice to class members, final approval by the Court. The defendants, including us, have denied and continue to deny all of plaintiffs' allegations of wrongdoing. There can be no assurance at this time that the settlement process will result in final Court approval. To the extent the case does not finally resolve through settlement, the defendants to the lawsuit, including us, continue to believe that plaintiffs' claims are without merit and intend to defend against the actions vigorously. Although we believe our directors and officer's insurance coverage is adequate, if our defense of the suit is unsuccessful, there can be no assurances that the insurance will substantially cover any resulting claim or that the premiums for directors and officers insurance will not be substantially higher in the future.

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

As of October 15, 2009, our officers, directors and holders of 5% or more of our outstanding common stock beneficially owned in excess of 79% of our common stock, assuming the full exercisability of all outstanding warrants. As a result, these stockholders, acting together, will be able to significantly influence all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with the interests of other stockholders, and they may act in a manner that advances their best interests and not necessarily those of other stockholders.

***Our certificate of incorporation, our bylaws and Delaware law contain provisions that could discourage another company from acquiring us and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions of Delaware law, where we are incorporated, our certificate of incorporation and bylaws may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace or remove our board of directors. These provisions include:

- authorizing the issuance of "blank check" preferred stock without any need for action by stockholders;
- providing for a classified board of directors with staggered terms;
- requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;
- eliminating the ability of stockholders to call special meetings of stockholders;
- prohibiting stockholder action by written consent; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

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

### **CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus and the documents we incorporate by reference in this prospectus contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the

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Exchange Act. We may, in some cases, use words such as “project,” “believe,” “anticipate,” “plan,” “expect,” “estimate,” “intend,” “should,” “would,” “could,” “potentially,” “will,” or “may,” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements may include statements about:

- our ability to complete clinical trials for our TH-302 and 2DG development programs;
- the completion and success of any clinical trials that we commence;
- the timing of results of our clinical trials;
- the costs and timing of obtaining drug supply for our pre-clinical and clinical activities;
- our receipt of regulatory approvals;
- our ability to establish and maintain intellectual property rights in our product candidates;
- uncertainties associated with obtaining and enforcing patents and other intellectual property rights;
- whether any product candidates that we are able to commercialize are safer or more effective than other marketed products, treatments or therapies;
- our research and development activities, including development of new product candidates, and projected expenditures;
- our ability to complete preclinical and clinical testing successfully for new product candidates that we may develop or license;
- our ability to have manufactured sufficient supplies of active pharmaceutical ingredient, or API, and drug product for clinical testing and commercialization;
- our ability to retain and hire necessary employees and appropriately staff our development programs;
- our cash needs; and
- our financial performance.

There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include those that we discuss in this prospectus under “[Risk Factors](#)” beginning on page 4 of this prospectus, as well those that we discuss in the documents we incorporate by reference in this prospectus. You should read these factors and the other cautionary statements made in this prospectus and in the documents we incorporate by reference into this prospectus as being applicable to all related forward-looking statements wherever they appear in this prospectus or the documents we incorporate by reference into this prospectus. 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.

### **USE OF PROCEEDS**

We will not receive any proceeds from the sales by the selling stockholders of the shares covered by this prospectus. The selling stockholders identified in this prospectus will receive the proceeds from such sale of shares. If the selling stockholders exercise, on a cash basis, all of the warrants underlying the shares being registered, we will receive approximately \$16,345,496. We will use such funds, if any, for working capital and general corporate purposes. We will not receive any proceeds from the exercise of warrants on a cashless basis.

### **SELLING STOCKHOLDERS**

On September 29, 2009, we entered into a Securities Purchase Agreement, or the 2009 Securities Purchase Agreement, with the selling stockholders, pursuant to which on the closing date of October 5, 2009, we sold an aggregate of 18,324,599 shares of our common stock and issued warrants to purchase up to 7,329,819 shares of our common stock. This prospectus covers the sale or other disposition by the purchasers under the 2009 Securities Purchase Agreement or their pledgees, donees, transferees and other successors-in-interest, collectively referred to throughout this prospectus as the selling stockholders, of up to the total number of shares of common stock issued to those selling stockholders pursuant to the 2009 Securities Purchase Agreement plus the total number of shares of common stock issuable upon exercise of the warrants issued to those selling stockholders. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares of our common stock, and the shares of our common stock underlying the warrants issued to the selling stockholders under the 2009 Securities Purchase Agreement.

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The warrants issued to the purchasers in the 2009 private placement became exercisable on October 5, 2009 at an exercise price of \$2.23 per share and expire on October 5, 2014. The exercise price and/or the number of shares of common stock issuable upon exercise of the warrants may be adjusted in certain circumstances and subject to certain limitations, including certain issuances of securities at a price equal to less than the then current exercise price, subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable.

We are registering the above-referenced shares to permit each of the selling stockholders and their pledgees, donees, transferees or other successors-in-interest that receive their shares after the date of this prospectus to resell or otherwise dispose of the shares in the manner contemplated under the “Plan of Distribution.”

The following table sets forth the name of each selling stockholder, the number of shares owned by each of the respective selling stockholders, the number of shares that may be offered under this prospectus and the number of shares of our common stock owned by the selling stockholders assuming all of the shares covered hereby are sold. The number of shares in the column “Number of Shares Being Offered” represents all of the shares that a selling stockholder may offer under this prospectus, and assumes the cash exercise of all the warrants for common stock. The selling stockholders may sell some, all or none of their shares. We do not know how long the selling stockholders will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale or other disposition of any of the shares. We also do not know if the selling stockholders will exercise any warrants. The shares covered hereby may be offered from time to time by the selling stockholders.

The information set forth below is based upon information obtained from the selling stockholders, information in our possession regarding the issuance of shares of common stock to the selling stockholders in connection with the 2009 private placement and information filed by the selling stockholders with the SEC. The percentages of shares owned after the offering set forth in the table below are based on 44,478,958 shares of our common stock outstanding as of October 15, 2009, including the shares of common stock issued in the 2009 private placement transaction, the shares of common stock issuable upon the cash exercise of all of the warrants issued in the 2009 private placement and the private placement that was completed on August 29, 2008.

In the table below, the number of shares of common stock owned before and after the offering represent shares directly held by each selling stockholder, except to the extent otherwise indicated in the footnotes. The footnotes also disclose all other shares beneficially owned by the selling stockholders. Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Exchange Act, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rule, beneficial ownership includes any shares as to which the selling stockholders has sole or shared voting power or investment power and also any shares, which the selling stockholders has the right to acquire within 60 days. The actual number of shares of common stock issuable upon the exercise of the warrants is subject to adjustment and could be materially less or more than the number estimated in the table. However, certain selling stockholders have contractually agreed to restrict their ability to exercise their warrants and receive shares of our common stock in the event that the number of shares of common stock held by them in the aggregate and their affiliates after such exercise would exceed 9.9% (and, in the case of Federated, 19.9%) of the then issued and outstanding shares of common stock as determined in accordance with Section 13(d) of the Exchange Act. Accordingly, the number of shares of common stock set forth in the table for the selling stockholders may exceed the number of shares of common stock that the selling stockholders could own beneficially at any given time through their ownership of shares of common stock and warrants.

Except as noted in the footnotes to the table below, the selling stockholders have not, within the past three years, had any position, office or other material relationship with us. In addition, except as set forth below, no selling stockholder is a broker-dealer or affiliated with a broker-dealer.

Name of Beneficial Owner	Shares of Common Stock Owned Prior to Offering (1)	Number of Shares being Offered		Shares Owned After Offering	
		Shares	Warrant Shares	Number	Percent
Alta BioPharma Partners III, GmbH & Co. Beteiligungs <sup>(2)</sup>	130,282	16,103	6,441	107,738	*
Alta BioPharma Partners III, L.P. <sup>(2)</sup>	1,939,908	239,768	95,907	1,604,233	7.2%
Alta Embarcadero BioPharma Partners III, LLC <sup>(2)</sup>	47,806	5,909	2,363	39,534	*
Baker Bros. Investments II, L.P. <sup>(3)</sup>	3,606	1,000	400	2,206	*
Baker Brothers Life Sciences, L.P. <sup>(3)</sup>	3,110,813	1,143,049	457,219	1,510,545	8.1%
Baker/Tisch Investments, L.P. <sup>(3)</sup>	27,255	11,423	4,569	11,263	*
14159, L.P. <sup>(3)</sup>	92,035	31,551	12,620	47,864	*
667, L.P. <sup>(3)</sup>	920,928	383,655	153,462	383,811	2.1%
Franklin M. Berger <sup>(4)</sup>	122,547	78,534	31,413	12,600	*
Biomedical Offshore Value Fund, Ltd. <sup>(5)</sup>	996,857	712,041	284,816	0	*
Biomedical Value Fund, L.P. <sup>(5)</sup>	1,935,077	1,382,198	552,879	0	*

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American Skandia Trust, Federated Aggressive Growth Portfolio <sup>(6)</sup>	317,609	226,864	90,745	0	*
Federated Kaufmann Fund II, a portfolio of Federated Insurance Series <sup>(7)</sup>	112,026	80,019	32,007	0	*
Federated Kaufmann Fund, a portfolio of Federated Equity Funds <sup>(8)</sup>	5,998,295	4,284,497	1,713,798	0	*
Federated Kaufmann Small Cap Fund, a portfolio of Federated Equity Funds <sup>(9)</sup>	901,910	644,222	257,688	0	*
Frazier Healthcare VI, L.P. <sup>(10)</sup>	5,497,381	3,926,701	1,570,680	0	*
HealthCare Ventures VIII, L.P. <sup>(11)</sup>	4,257,775	1,570,680	628,272	2,058,823	10.9%
Opus Point Healthcare (Low Net) Fund, L.P. <sup>(12)</sup>	73,298	52,356	20,942	0	*
Opus Point Healthcare Innovations Fund, L.P. <sup>(12)</sup>	147,912	104,712	41,884	1,316	*
Opus Point Healthcare Value Fund, L.P. <sup>(12)</sup>	146,696	104,712	41,884	100	*
Panacea Fund, LLC <sup>(13)</sup>	293,193	209,424	83,769	0	*
Polar Capital Funds PLC – Healthcare Opportunities Fund <sup>(14)</sup>	293,193	209,424	83,769	0	*
David L. Anderson <sup>(15)</sup>	86,483	13,779	5,511	67,193	*
Yu-Ying Chen <sup>(16)</sup>	5,146	785	314	4,047	*
Tench Coxe <sup>(17)</sup>	215,848	151,896	60,758	3,194	*
David E. Sweet <sup>(18)</sup>	38,026	9,497	3,798	24,731	*
Diane J. Naar <sup>(19)</sup>	3,157	785	314	2,058	*
Patricia Tom <sup>(20)</sup>	2,913	1,570	628	715	*
Robert Yin <sup>(21)</sup>	2,939	392	156	2,391	*
William H. Younger, Jr. <sup>(22)</sup>	176,829	66,274	26,509	84,046	*
Sutter Hill Ventures <sup>(23)</sup>	5,030,184	1,143,734	457,493	3,428,957	12.9%
Anvest, L.P. <sup>(24)</sup>	23,456	13,779	5,511	4,166	*
Gregory P. Sands and Sarah J.D. Sands as Trustees of the Gregory P. and Sarah J.D. Sands Trust Agreement Dated 2/24/99 <sup>(25)</sup>	103,138	24,679	9,871	68,588	*
Andrew T. Sheehan and Nicole J. Sheehan as Trustees of the Sheehan 2003 Trust <sup>(26)</sup>	59,471	13,156	5,262	41,053	*
Saunders Holdings, L.P. <sup>(27)</sup>	71,386	17,443	6,977	46,966	*
James N. White and Patricia A. O' Brien as Trustees of the White Family Trust U/A/D 4/3/97 <sup>(28)</sup>	161,763	37,619	15,047	109,097	*
Jeffrey W. Bird and Christina R. Bird as Trustees of the Jeffrey W. and Christina R. Bird Trust Agreement Dated 10/31/00 <sup>(29)</sup>	148,453	34,697	13,878	99,878	*
G. Leonard Baker, Jr. and Mary Anne Baker, Co-Trustees of the Baker Revocable Trust U/A/D 2/3/03 <sup>(30)</sup>	101,044	23,123	9,249	68,672	*
James C. Gaither, Trustee of The Gaither Revocable Trust U/A/D 9/28/2000 <sup>(31)</sup>	30,789	17,472	6,988	6,329	*
Three Arch Associates III, L.P. <sup>(32)</sup>	165,563	53,424	21,369	90,770	*
Three Arch Partners III, L.P. <sup>(32)</sup>	3,079,649	993,696	397,478	1,688,475	2.9%
V2M Life Sciences Fund, L.P. <sup>(33)</sup>	329,800	39,267	15,706	274,827	*
John G. Curd, M.D. <sup>(34)</sup>	163,658	26,178	10,471	127,009	*
Stewart M. Kroll <sup>(35)</sup>	56,216	5,235	2,094	48,887	*
Mark D. Matteucci, Ph.D. <sup>(36)</sup>	624,289	164,921	65,968	393,400	2.1%
Harold E. Selick, Ph.D. <sup>(37)</sup>	426,587	52,356	20,942	353,289	1.9%

\* Less than 1%.

- (1) The number of shares presented in this table as owned prior to this offering by any selling stockholder includes all shares of common stock issuable upon the cash exercise of the warrants issued to such stockholder in the 2009 private placement, as evidenced by the warrant shares indicated across from each stockholder in the column "Warrant Shares," all shares of common stock issuable upon the cash exercise of the warrants issued in the private placement of our common stock which was completed on August 29, 2008 and all shares issuable upon the cash exercise of options exercisable within 60 days of October 15, 2009.
- (2) Jean Deleage, Edward Penhoet, Edward Hurwitz and Farah Champsy of Alta BioPharma Management III LLC share voting and investment control over these securities. The selling stockholder's address is One Embarcadero Center, Suite 3700, San Francisco, CA 94111.

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- (3) Felix J. Baker and Julian C. Baker have voting and investment control over these securities. The selling stockholder's address is 667 Madison Ave., 21st Floor, New York, NY 10065.
- (4) The selling stockholder's address is 257 Park Ave. South, 15th Floor, New York, NY 10010.
- (5) Each of Great Point Partners, LLC, Dr. Jeffrey Jay and Mr. David Kroin share voting and dispositive power over the shares of common stock of the Company held by Biomedical Value Fund L.P. and Biomedical Offshore Value Fund, Ltd. (collectively, "Biomedical"). Each of Dr. Jay and Mr. Kroin disclaim beneficial ownership of such shares. The address for Biomedical is c/o Great Point Partners, 165 Mason St., 3rd Floor, Greenwich, CT 06830.
- (6) American Skandia Trust, Federated Aggressive Growth Portfolio ("ASTAG") is a portfolio of Advanced Series Trust, a registered investment company. ASTAG's investment advisors are Prudential Investments LLC and AST Investment Services, Inc., which have delegated daily management of the fund's assets to Federated Equity Management Company of Pennsylvania ("FEMCPA") as sub-advisor. The parent holding company of ASTAG's sub-advisor is Federated Investors Inc. ("FII"). ASTAG's sub-advisor, FEMCPA, has delegated daily management of the fund's assets to Federated Global Investment Management Corp. ("FGIMC"), as sub-sub-advisor. While the officers and directors of FEMCPA have dispositive power over ASTAG's portfolio securities, they customarily delegate this dispositive power, and therefore the day-to-day dispositive decisions are made by the portfolio managers of ASTAG, currently, Lawrence Auriana and Hans P. Utsch. Messrs. Auriana and Utsch disclaim any beneficial ownership of these securities. With respect to voting power, ASTAG has delegated the authority to vote proxies to FEMCPA. FEMCPA has established a Proxy Voting Committee to cast proxy votes on behalf of ASTAG in accordance with proxy voting policies and procedures approved by ASTAG. Securities are held of record by Hare & Co. on behalf of ASTAG. ASTAG is affiliated with Federated Financial Services, Inc., Federated Securities Corp. and Edgewood Services, Inc., each of which is a member of FINRA. ASTAG has represented to us that the shares and warrants held by it were purchased in the ordinary course of business and that at the time of purchase of the shares and warrants held by it, it was not aware of any agreements or understandings, directly or indirectly, with any person to distribute the shares held by it or the common stock issuable upon exercise of the warrants held by it. The selling stockholder's address is 140 E. 45th St., New York, NY 10017.
- (7) Federated Kaufmann Fund II ("FKFII") is a portfolio of Federated Insurance Series, a registered investment company. The parent holding company of FKF's advisors is Federated Investors Inc. ("FII"). FKFII's advisor is Federated Equity Management Company of Pennsylvania ("FEMCPA") which has delegated daily management of the fund's assets to Federated Global Investment Management Corp. ("FGIMC"), as subadvisor. While the officers and directors of FEMCPA have dispositive power over FKFII's portfolio securities, they customarily delegate this dispositive power, and therefore the day-to-day dispositive decisions are made by the portfolio managers of FKFII, currently, Lawrence Auriana and Hans P. Utsch. Messrs. Auriana and Utsch disclaim any beneficial ownership of these securities. With respect to voting power, FKFII has delegated the authority to vote proxies to FEMCPA. FEMCPA has established a Proxy Voting Committee to cast proxy votes on behalf of FKFII in accordance with proxy voting policies and procedures approved by FKFII. Securities are held of record by Turnseal & Co. on behalf of FKFII. FKFII is affiliated with Federated Financial Services, Inc., Federated Securities Corp. and Edgewood Services, Inc., each of which is a member of FINRA. FKFII has represented to us that the shares and warrants held by it were purchased in the ordinary course of business and that at the time of purchase of the shares and warrants held by it, it was not aware of any agreements or understandings, directly or indirectly, with any person to distribute the shares held by it or the common stock issuable upon exercise of the warrants held by it. The selling stockholder's address is 140 E. 45th St., New York, NY 10017.
- (8) Federated Kaufmann Fund ("FKF") is a portfolio of Federated Equity Funds, a registered investment company. The parent holding company of FKF's advisors is Federated Investors Inc. ("FII"). FKF's advisor is Federated Equity Management Company of Pennsylvania ("FEMCPA") which has delegated daily management of the fund's assets to Federated Global Investment Management Corp. ("FGIMC"), as subadvisor. While the officers and directors of FEMCPA have dispositive power over FKF's portfolio securities, they customarily delegate this dispositive power, and therefore the day-to-day dispositive decisions are made by the portfolio managers of FKF, currently, Lawrence Auriana and Hans P. Utsch. Messrs. Auriana and Utsch disclaim any beneficial ownership of these securities. With respect to voting power, FKF has delegated the authority to vote proxies to FEMCPA. FEMCPA has established a Proxy Voting Committee to cast proxy votes on behalf of FKF in accordance with proxy voting policies and procedures approved by FKFII. Securities are held of record by Playback & Co. on behalf of FKF. FKF is affiliated with Federated Financial Services, Inc., Federated Securities Corp. and Edgewood Services, Inc., each of which is a member of FINRA. FKF has represented to us that the shares and warrants held by it were purchased in the ordinary course of business and that at the time of purchase of the shares and warrants held by it, it was not aware of any agreements or understandings, directly or indirectly, with any person to distribute the shares held by it or the common stock issuable upon exercise of the warrants held by it. The selling stockholder's address is 140 E. 45th St., New York, NY 10017.
- (9) Federated Kaufmann Small Cap Fund ("FKSCF") is a portfolio of Federated Equity Funds, a registered investment company. The parent holding company of FKF's advisors is Federated Investors Inc. ("FII"). FKSCF's advisor is Federated Equity Management Company of Pennsylvania ("FEMCPA") which has delegated daily management of the fund's assets to Federated Global Investment Management Corp. ("FGIMC"), as subadvisor. While the officers and directors of FEMCPA have dispositive power over FKSCF's



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- portfolio securities, they customarily delegate this dispositive power, and therefore the day-to-day dispositive decisions are made by the portfolio managers of FKSCF, currently, Lawrence Auriana and Hans P. Utsch. Messrs. Auriana and Utsch disclaim any beneficial ownership of these securities. With respect to voting power, FKSCF has delegated the authority to vote proxies to FEMCPA. FEMCPA has established a Proxy Voting Committee to cast proxy votes on behalf of FKSCF in accordance with proxy voting policies and procedures approved by FKSCF. Securities are held of record by Boathorn & Co. on behalf of FKSCF. FKSCF is affiliated with Federated Financial Services, Inc., Federated Securities Corp. and Edgewood Services, Inc., each of which is a member of FINRA. FKSCF has represented to us that the shares and warrants held by it were purchased in the ordinary course of business and that at the time of purchase of the shares and warrants held by it, it was not aware of any agreements or understandings, directly or indirectly, with any person to distribute the shares held by it or the common stock issuable upon exercise of the warrants held by it. The selling stockholder's address is 140 E. 45th St., New York, NY 10017.
- (10) FHM VI, L.L.C., a Delaware limited liability company, is the general partner of FHM VI, L.P., which is the general partner of Frazier Healthcare VI, L.P. FHM VI, L.L.C. and FHM VI, L.P. share voting and dispositive power and may be deemed to beneficially own the securities held by Frazier Healthcare VI, L.P. The members of FHM VI, LLC are Alan D. Frazier, Nader Naini, Trevor Moody, Nathan Emery, James Topper, Patrick Heron, Robert More and Thomas S. Hodge (the "Investment Committee"). Decisions to purchase or sell securities held by Frazier Healthcare VI, L.P. are made by a majority vote of the Investment Committee. The members of the Investment Committee disclaim beneficial ownership in these securities except as to their pecuniary interest therein. The selling stockholder's address is 601 Union St., Suite 3200, Seattle, WA 98101.
- (11) The general partner of the selling stockholder is HealthCare Partners VIII, L.P. ("HCP VIII"), and the general partner of HCP VIII is HealthCare Partners VIII, LLC ("HCP VIII LLC"). James H. Cavanaugh, Ph.D., Christopher Mirabelli, Ph.D., Harold R. Werner, John W. Littlechild and Augustine Lawlor are the managing directors of HCP VIII LLC. Each of HCP VIII, HCP VIII LLC, Dr. Cavanaugh, Dr. Mirabelli, Mr. Werner, Mr. Littlechild and Augustine Lawlor share voting and investment power over these securities. The selling stockholder's address is 44 Nassau St., Princeton, NJ 08542.
- (12) Michael S. Weiss and Lindsay A. Rosenwald, M.D. of Opus Point Healthcare Fund Management LLC share voting and investment control over these securities. Opus Point Healthcare Fund Management LLC is affiliated with Paramount Capital, Inc., a FINRA member. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 787 7th Ave., 48th Floor, New York, NY 10019.
- (13) Charles Polsky, Michael Resnick and Jack Polsky, officers of William Harris Investors, Inc., the manager of Panacea Fund, LLC, share voting and investment power over these securities. The selling stockholder's address is 191 N. Wacker Dr., Suite 1500, Chicago, IL 60606.
- (14) Polar Capital LLP is the investment manager of Polar Capital Funds PLC – Healthcare Opportunities Fund and shares voting and dispositive power over these shares with Nexus Gemini LP. Securities are held of record by NorTrust Nominees Limited on behalf of Healthcare Opportunities Fund. Daniel Mahony and Gareth Powell are the controlling partners of Polar Capital LLP and as such may be deemed to possess voting and investment control over the securities held by Polar Capital Funds PLC – Healthcare Opportunities Fund. The selling stockholder's address is 4 Matthew Parker St., London SW1H 9NP, England.
- (15) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO David L. Anderson. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Does not include 6,837 shares held in The Anderson Living Trust, a trust for Mr. Anderson's benefit, 4,166 shares held by Anvest, L.P., a selling stockholder of which Mr. Anderson is a general partner, or any securities for which Mr. Anderson may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Mr. Anderson is a managing director of the general partner of Sutter Hill Ventures. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (16) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO Yu-Ying Chen. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Ms. Chen is an employee of the general partner of Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.



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- (17) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO Tenche Coxo. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Does not include 335,368 shares and warrants to purchase 109,437 shares held by The Coxo Revocable Trust over which Tench Coxo and Simone Otus Coxo, as Co-Trustees, have voting and investment control, or any securities for which Mr. Coxo may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Mr. Coxo is a managing director of the general partner of Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (18) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO David E. Sweet. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Does not include 2,302 shares held by The David and Robin Sweet Living Trust, of which Mr. Sweet is a trustee, or any securities for which Mr. Sweet may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Mr. Sweet is a managing director of the general partner of Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (19) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO Diane J. Naar. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Ms. Naar is an employee of Sutter Hill Management Co., LLC, an affiliate of Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (20) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO Patricia Tom. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Ms. Tom is an employee of Sutter Hill Management Co., LLC, an affiliate of Sutter Hill Ventures. Does not include 2,941 shares and 1,176 warrants to purchase shares held by Patricia Tom individually. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (21) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO Robert Yin. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Does not include 284 shares held by a trust for the benefit of Mr. Yin. Mr. Yin is an employee of Sutter Hill Management Co., LLC, an affiliate of Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (22) Includes securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO William H. Younger, Jr. The SHV Profit Sharing Plan is affiliated with Sutter Hill Ventures. Does not include 21,507 shares held in the Younger Living Trust of which Mr. Younger is a trustee, 56,255 shares and warrants to purchase 22,502 shares held by Yovest, L.P., of which Mr. Younger is the trustee of a trust which is the general partner or any securities for which Mr. Younger may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Mr. Younger is a managing director of the general partner of Sutter Hill Ventures. Wells Fargo Bank, N.A. is directed by any authorized signer for the SHV Profit Sharing Plan and disclaims voting and investment control over these securities and any beneficial ownership of the securities. Wells Fargo Bank, N.A., is affiliated with a number of registered broker-dealers. The selling stockholder has represented to us that it acquired the shares of common

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- stock and the warrants in the 2009 private placement in the ordinary course of business. At the time of acquisition of such warrants and shares, the selling stockholder had no agreements or understandings, directly or indirectly, with any other person to distribute such warrants or shares. The selling stockholder's address is 600 California St., 12th Floor, MAC A019-120/Inst. Trust Serv., San Francisco, CA 94108.
- (23) The managing directors of the general partner of the selling stockholder have voting and investment control over these securities. Includes 10,028 shares held by Sutter Hill Entrepreneurs Fund (QP), L.P. and 3,960 shares held by Sutter Hill Entrepreneurs Fund (AI), L.P. Does not include shares beneficially owned by the managing directors of the general partner of the selling stockholder or shares held for the benefit of certain participants in the SHV Profit Sharing Plan. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (24) David L. Anderson, a selling stockholder and a managing director of the general partner of Sutter Hill Ventures, is the general partner of Anvest, L.P. and has voting and investment control over these securities. Mr. Anderson disclaims beneficial ownership in these securities except as to his pecuniary interest therein. Does not include securities held by Wells Fargo Bank, N.A FBO SHV Profit Sharing Plan FBO David L. Anderson, shares held in The Anderson Living Trust, a trust for Mr. Anderson's benefit, or any securities for which Mr. Anderson may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Each of G. Leonard Baker, Jr., Jeffrey W. Bird, Tench Coxo, James C. Gaither, Gregory P. Sands, Michael L. Speiser, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Anvest, L.P. with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (25) Gregory P. Sands and Sarah J.D. Sands, as Trustees, have voting and investment control over these securities. Mr. Sands is a managing director of the general partner of Sutter Hill Ventures. Mr. Sands disclaims beneficial ownership in these securities except as to his pecuniary interest therein. Does not include 4,014 shares held in the Gregory P. Sands Charitable Remainder Unitrust of which Mr. Sands is the trustee or any securities for which Mr. Sands may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Mr. Sands is a managing director of the general partner of Sutter Hill Ventures. Each of David L. Anderson, G. Leonard Baker, Jr., Jeffrey W. Bird, Tench Coxo, James C. Gaither, Michael L. Speiser, Gregory P. Sands, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Mr. Sands with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (26) Andrew T. Sheehan and Nicole J. Sheehan, as Trustees, have voting and investment control over these securities. Mr. Sheehan is a managing director of the general partner of Sutter Hill Ventures. Mr. Sheehan disclaims beneficial ownership in these securities except as to his pecuniary interest therein. Each of David L. Anderson, G. Leonard Baker, Jr., Jeffrey W. Bird, Tench Coxo, James C. Gaither, Gregory P. Sands, Michael L. Speiser, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Mr. Sheehan with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (27) G. Leonard Baker, Jr., and Mary Anne Baker, as general partners of the selling stockholder, have voting and investment control over these securities. Mr. Baker is a managing director of the general partner of Sutter Hill Ventures. Mr. Baker disclaims beneficial ownership in these securities except as to his pecuniary interest therein. Does not include 77,421 shares and warrants to purchase 23,623 shares held by G. Leonard Baker, Jr. and Mary Anne Baker, Co-Trustees of the Baker Revocable Trust U/A/D 2/3/03. Each of David L. Anderson, Jeffrey W. Bird, Tench Coxo, James C. Gaither, Gregory P. Sands, Andrew T. Sheehan, Michael L. Speiser, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Mr. Baker with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (28) James N. White and Patricia O'Brien, as Trustees, have voting and investment control over these securities. Mr. White is a managing director of the general partner of Sutter Hill Ventures. Mr. White disclaims beneficial ownership in these securities except as to his pecuniary interest therein. Does not include 4,076 shares held for Mr. White's benefit in the SHV Profit Sharing Plan or any securities for which Mr. White may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Mr. White is a managing director of the general partner of Sutter Hill Ventures. Each of David L. Anderson, G. Leonard Baker, Jr., Jeffrey W. Bird, Tench Coxo, James C. Gaither, Gregory P. Sands, Andrew T. Sheehan, Michael L. Speiser, David E. Sweet, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Mr. White with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (29) Jeffrey W. Bird and Christina R. Bird, as Trustees, have voting and investment control over these securities. Dr. Bird is a managing director of the general partner of Sutter Hill Ventures and a director of the Company. Dr. Bird disclaims beneficial ownership in these securities except as to his pecuniary interest therein. Does not include 15,971 shares issuable upon the exercise of outstanding director's options held by Dr. Bird exercisable within 60 days of October 15, 2009 or 919 shares held for Dr. Bird's benefit in the SHV Profit Sharing Plan. Each of David L. Anderson, G. Leonard Baker, Jr., Tench Coxo, James C. Gaither, Gregory P. Sands, Andrew T. Sheehan, Michael L. Speiser, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Dr. Bird with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.

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- (30) G. Leonard Baker, Jr. and Mary Anne Baker, as Co-Trustees, have voting and investment control over these securities. Mr. Baker is a managing director of the general partner of Sutter Hill Ventures. Mr. Baker disclaims beneficial ownership in the securities held by the trust except as to his pecuniary interest therein. Does not include 3,840 shares held by Mr. Baker individually or 36,122 shares and warrants to purchase 10,844 shares held by Saunders Holdings, L.P., of which G. Leonard Baker, Jr. and Mary Anne Baker are general partners. Each of David L. Anderson, Jeffrey W. Bird, Tench Coxé, James C. Gaither, Gregory P. Sands, Andrew T. Sheehan, Michael L. Speiser, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Mr. Baker with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (31) James C. Gaither, as Trustee, has voting and investment control over these securities. Mr. Gaither is a managing director of the general partner of Sutter Hill Ventures. Mr. Gaither disclaims beneficial ownership in the securities held by the trust except as to his pecuniary interest therein. Does not include 32,615 shares and warrants to purchase 11,729 shares held by Tallack Partners, L.P., of which Mr. Gaither is the general partner, or any securities for which Mr. Gaither may be deemed to have beneficial ownership due to his role with Sutter Hill Ventures. Each of David L. Anderson, G. Leonard Baker, Jr., Jeffrey W. Bird, Tench Coxé, Gregory P. Sands, Andrew T. Sheehan, Michael L. Speiser, David E. Sweet, James N. White, Robert Yin and William H. Younger, Jr. each have power of attorney to act on behalf of Mr. Gaither with respect to these securities. The selling stockholder's address is 755 Page Mill Rd., Suite A-200, Palo Alto, CA 94304.
- (32) Wilfred E. Jaeger, as Managing Member of Three Arch Management III, LLC, the general partner of the selling stockholder, has voting and investment control over these securities. Dr. Jaeger is a director of the Company. Does not include 23,330 shares issuable upon the exercise of outstanding director's options held by Dr. Jaeger exercisable within 60 days of October 15, 2009. The selling stockholder's address is 3200 Alpine Rd., Portola Valley, CA 94028.
- (33) Dennis McCoy and Misha Petkevich are managing members of BladeRock Capital, LLC, the general partner of the selling stockholder, and have voting and investment control over these securities. The selling stockholder's address is 121 Mount Vernon St., Boston, MA 02108.
- (34) Dr. Curd is our President and Chief Medical Officer. Includes 41,445 shares issuable upon the exercise of outstanding options exercisable within 60 days of October 15, 2009. The selling stockholder's address is c/o Threshold Pharmaceuticals, Inc., 1300 Seaport Blvd., Suite 500, Redwood City, CA 94063.
- (35) Mr. Kroll is our Vice President of Biostatistics and Clinical Operations. Includes 23,807 shares issuable upon the exercise of outstanding options exercisable within 60 days of October 15, 2009. The selling stockholder's address is c/o Threshold Pharmaceuticals, Inc., 1300 Seaport Blvd., Suite 500, Redwood City, CA 94063.
- (36) Dr. Matteucci is our Senior Vice President, Discovery Research. Includes 25,694 shares issuable upon the exercise of outstanding options exercisable within 60 days of October 15, 2009. The selling stockholder's address is c/o Threshold Pharmaceuticals, Inc., 1300 Seaport Blvd., Suite 500, Redwood City, CA 94063.
- (37) Dr. Selick is our Chief Executive Officer. Includes 70,336 shares issuable upon the exercise of outstanding options exercisable within 60 days of October 15, 2009. The selling stockholder's address is c/o Threshold Pharmaceuticals, Inc., 1300 Seaport Blvd., Suite 500, Redwood City, CA 94063.

## DESCRIPTION OF CAPITAL STOCK

*The description below of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws. These documents are filed as exhibits to the registration statement of which this prospectus is a part.*

Our amended and restated certificate of incorporation authorizes the issuance of up to 50,000,000 shares of common stock, par value \$0.001 per share, and 2,000,000 shares of preferred stock, par value \$0.001 per share. The rights and preferences of the preferred stock may be established from time to time by our board of directors. As of October 15, 2009, we had 33,560,918 shares of common stock outstanding, held by 114 stockholders of record as of such date. As of October 15, 2009, there were no shares of preferred stock outstanding.

### Common Stock

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, except matters that relate only to one or more of the series of preferred stock, and each holder does not have cumulative voting rights. Accordingly, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose.

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by the board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Holders of common stock have no preemptive or conversion rights or other subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are, and the shares of common stock offered by us in this offering, when issued and paid for, will be fully paid and nonassessable. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock which we may designate in the future.

### Preferred Stock

Our board of directors is authorized, subject to any limitations prescribed by law, without stockholder approval, to issue up to an aggregate of 2,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions granted to or imposed upon the preferred stock, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of holders of any preferred stock that may be issued in the future. Issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could have the effect of delaying, deferring or preventing a change in control of us. We have no present plans to issue any shares of preferred stock, but 200,000 shares of preferred stock have been designated as "Series A Participating Preferred Stock" to satisfy our obligations with respect to the Rights described below.

### Warrants

As of October 15, 2009, we had outstanding warrants to purchase an aggregate of 3,588,221 shares of our common stock with an exercise price of \$1.86 per share, and warrants to purchase an aggregate of 7,329,819 shares of our common stock with an exercise price of \$2.23 per share. The exercise price and/or the number of shares of common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including certain issuances of securities at a price equal to less than the then current exercise price, subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable.

### Rights Agreement

In August 2006, our board of directors declared a dividend of one preferred stock purchase right, a Right, for each share of common stock outstanding as of the close of business on August 23, 2006. The Rights currently trade with, and are inseparable from, the common stock. The Rights will become exercisable only if a person or group (i) acquires beneficial ownership of 15% or more of our outstanding common stock or (ii) commences a tender or exchange offer that would result in that person or group becoming a beneficial owner of 15% or more of our outstanding common stock. Each Right allows its holder to purchase from us one one-thousandth of a share of Series A Participating Preferred Stock at a purchase price of \$25.00 per one-thousandth of a preferred share, subject to adjustment. The Rights expire on August 8, 2016, unless we extend the expiration date, redeem or exchange the Rights on an earlier date or the Rights expire upon consummation of certain mergers, consolidations or sales of assets. Effective

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July 10, 2008 and September 29, 2009, we amended the terms of the Rights to ensure that they would not become exercisable solely by virtue of our private placements of securities completed on August 29, 2008 and October 5, 2009, respectively.

### **Effect of Certain Provisions of our Amended and Restated Certificate of Incorporation and Bylaws and the Delaware Anti-Takeover Statute**

#### *Amended and Restated Certificate of Incorporation and Bylaws*

Some provisions of Delaware law and our amended and restated certificate of incorporation and bylaws contain provisions that could make the following transactions more difficult:

- acquisition of us by means of a tender offer;
- acquisition of us by means of a proxy contest or otherwise; or
- removal of our incumbent officers and directors.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids and to promote stability in our management. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

- *Undesignated Preferred Stock.* The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue one or more series of preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.
- *Stockholder Meetings.* Our charter documents provide that a special meeting of stockholders may be called only by the chairman of our board of directors or by our president, or by a resolution adopted by a majority of our board of directors.
- *Requirements for Advance Notification of Stockholder Nominations and Proposals.* Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of the board of directors.
- *Elimination of Stockholder Action by Written Consent.* Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.
- *Amendment of Bylaws.* Any amendment of our bylaws by our stockholders requires approval by holders of at least 66<sup>2/3</sup>% of our then outstanding common stock, voting together as a single class.
- *Staggered Board of Directors.* Our amended and restated certificate of incorporation provide for the division of our board of directors into three classes, as nearly equal in size as possible, with staggered three-year terms. Under our amended and restated certificate of incorporation and amended and restated bylaws, any vacancy on the board of directors, including a vacancy resulting from an enlargement of the board of directors, may only be filled by vote of a majority of the directors then in office. The classification of the board of directors and the limitations on the removal of directors and filling of vacancies would have the effect of making it more difficult for a third party to acquire control of us, or of discouraging a third party from acquiring control of us.

#### **Delaware Anti-Takeover Statute**

We are subject to Section 203 of the General Corporation Law of the State of Delaware. This law prohibits a publicly held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned by persons who are directors and also officers and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

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Section 203 defines “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of our assets involving the interested stockholder;
- in general, any transaction that results in the issuance or transfer by us of any of our stock to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

### **Limitation of Liability**

Our amended and restated certificate of incorporation provides that no director shall be personally liable to us or to our stockholders for monetary damages for breach of fiduciary duty as a director, except that the limitation shall not eliminate or limit liability to the extent that the elimination or limitation of such liability is not permitted by the General Corporation Law of the State of Delaware as the same exists or may hereafter be amended.

### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is BNY Mellon Shareowner Services, P.O. Box 358016, Pittsburgh, PA 15252-8016.

### **PLAN OF DISTRIBUTION**

The selling stockholders and their pledgees, donees, transferees or successors-in-interest may, from time to time, offer and sell or otherwise dispose of any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved, and the maximum commission or discount to be received by any member of the Financial Industry Regulatory Authority, Inc. (FINRA) or independent broker-dealer will not be greater than 8% of the initial gross proceeds from the sale of any security being sold. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a selling stockholder. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The selling stockholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and

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sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act supplementing or amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act supplementing or amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay all fees and expenses incident to the registration of the shares of common stock. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by any selling stockholder. If we are notified by any selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the selling stockholders use this prospectus for any sale of the shares of common stock, they will be subject to the prospectus delivery requirements of the Securities Act.

The anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of our common stock and activities of the selling stockholders.

### **LEGAL MATTERS**

The validity of the securities offered hereby has been passed upon for us by Morrison & Foerster LLP, Palo Alto, California.

### **EXPERTS**

The consolidated financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2008 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company’s ability to continue as a going concern as described in Note 1 to the consolidated financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

### **INCORPORATION OF INFORMATION BY REFERENCE**

The SEC allows us to “incorporate by reference” the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and certain information that we will later file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below as well as any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act from the date of the initial registration statement and prior to the effectiveness of this registration statement, and any filings made after the date of this prospectus until we sell all of the securities under this prospectus, except that we do not incorporate any document or portion of a document that was furnished and deemed by the rules of the SEC not to have been filed:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2008, filed with the SEC on March 13, 2009;
- The portions of our definitive Proxy Statement on Schedule 14A for our 2009 Annual Meeting of Stockholders, filed with the SEC on April 9, 2009, that are incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2008;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2009, filed with the SEC on May 7, 2009;
- Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009, filed with the SEC on August 6, 2009;
- Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2008, filed with the SEC on November 5, 2009;
- Our Current Report on Form 8-K filed with the SEC on January 14, 2009;
- Our Current Report on Form 8-K filed with the SEC on September 21, 2009;



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- Our Current Report on Form 8-K filed with the SEC on September 30, 2009;
- Our Current Report on Form 8-K filed with the SEC on October 6, 2009;
- Our Current Report on Form 8-K filed with the SEC on October 9, 2009;
- Our Current Report on Form 8-K filed with the SEC on October 19, 2009;
- Our Current Report on Form 8-K filed with the SEC on October 23, 2009; and
- Our Current Report on Form 8-K filed with the SEC on November 9, 2009.

All other reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14, and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of this offering shall be deemed to be incorporated by reference in this prospectus and to be part hereof from the date of filing of such reports and other documents.

We hereby undertake to provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon written or oral request of any such person, a copy of any and all of the information that has been or may be incorporated by reference in this prospectus, other than exhibits to such documents. Requests for such copies should be directed to our Investor Relations Department at 1300 Seaport Boulevard, Suite 500, Redwood City, California 94063, Telephone (650) 474-8200.

### **WHERE YOU CAN FIND ADDITIONAL INFORMATION**

We are a public company and file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at (800) SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available, at no charge, to the public at the SEC's web site at <http://www.sec.gov>.