

CYTOKINETICS INC
Form S-3
June 14, 2005

Table of Contents

As filed with the Securities and Exchange Commission on June 14, 2005
Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT
Under
The Securities Act of 1933

CYTOKINETICS, INCORPORATED

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

94-3291317
(I.R.S. Employer
Identification Number)

280 East Grand Avenue
South San Francisco, CA 94080
(650) 624-3000

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

James Sabry, M.D., Ph.D.
President and Chief Executive Officer
Cytokinetics, Incorporated
280 East Grand Avenue
South San Francisco, CA 94080
(650) 624-3000

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:
Michael O. Donnell, Esq.
Martin Waters, Esq.
Gavin McCraley, Esq.
Wilson Sonsini Goodrich & Rosati
Professional Corporation
650 Page Mill Road
Palo Alto, CA 94304
(650) 493-9300

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price per Unit	Proposed Maximum Offering Price(1)	Amount of Registration Fee
Common Stock, \$0.001 par value per share(2)				
Preferred Stock, \$0.001 par value per share(2)				
Warrants(3)				
Total(4)	\$ 100,000,000(4)	100%(5)	\$ 100,000,000	\$ 11,770

- (1) These figures are estimates made solely for the purpose of calculating the registration fee pursuant to Rule 457 under the Securities Act of 1933, as amended.
- (2) In addition to any securities that may be registered hereunder, we are also registering an indeterminate number of shares of common stock or preferred stock as may be issued upon conversion or exchange of the securities issued directly hereunder. No separate consideration will be received for any shares of common stock or preferred stock so issued upon conversion or exchange.
- (3) Includes warrants to purchase common stock and warrants to purchase preferred stock.
- (4) The securities registered hereunder may be sold separately, or as units with other securities registered hereby. The proposed maximum offering price per unit will be determined by us in connection with the issuance of the securities. In no event will the aggregate offering price of all securities issued from time to time pursuant to this Registration Statement exceed \$100,000,000. The aggregate amount of common stock registered hereunder is further limited to that which is permissible under Rule 415(a)(4) under the Securities Act, to the extent

applicable.

- (5) We will determine the proposed maximum offering price per unit in connection with the issuance of the securities.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission acting pursuant to said Section 8(a) may determine.

Table of Contents

PROSPECTUS

The Information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell securities and is not soliciting an offer to buy securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JUNE 14, 2005

\$100,000,000

Cytokinetics, Incorporated

**COMMON STOCK
PREFERRED STOCK
WARRANTS**

From time to time, we may sell any of the securities listed above. All of the securities listed above may be sold separately or as units with other securities. We will specify in an accompanying prospectus supplement the terms of any offering. Our common stock is traded on the Nasdaq National Market under the trading symbol CYTK. On June 13, 2005 the last reported sale price of our common stock on the Nasdaq National Market was \$5.18 per share.

You should read this prospectus, any prospectus supplement and the documents incorporated by reference in this prospectus and any prospectus supplement carefully before you invest. **This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.**

Investing in our securities involves a high degree of risk. You should carefully consider the Risk Factors beginning on page 2 of this prospectus before you make an investment decision.

The securities offered by this prospectus may be offered in amounts, at prices and at terms determined at the time of the offering and may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. We will set forth the names of any underwriters or agents in the accompanying prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution. The net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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 _____, 200

TABLE OF CONTENTS

<u>Cytokinetics, Incorporated</u>	1
<u>Risk Factors</u>	2
<u>Disclosure Regarding Forward-Looking Statements</u>	21
<u>Use of Proceeds</u>	22
<u>Ratio Of Earnings Available To Cover Fixed Charges</u>	22
<u>Description of Capital Stock</u>	23
<u>Description of the Warrants</u>	27
<u>Plan of Distribution</u>	29
<u>Legal Matters</u>	31
<u>Experts</u>	31
<u>Where You Can Find More Information</u>	31
<u>Information Incorporated by Reference</u>	32
<u>EXHIBIT 5.1</u>	
<u>EXHIBIT 12.1</u>	
<u>EXHIBIT 23.1</u>	

No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. Neither the delivery of this prospectus or any prospectus supplement nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement is correct as of any date subsequent to the date hereof or of such prospectus supplement.

Table of Contents

SUMMARY

The following summary is qualified in its entirety by the more detailed information, including our consolidated financial statements and related notes incorporated in this prospectus by reference. You should carefully consider the information set forth in this entire prospectus, including the Risk Factors section, the applicable prospectus supplement for such securities and the other documents we refer to and incorporate by reference. Unless the context otherwise requires, the terms Cytokinetics, we, us and our refer to Cytokinetics, Incorporated, a Delaware corporation.

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus, in one or more offerings, up to an aggregate offering price of \$100,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell any securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of those securities. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement, including the risk factors, together with the additional information described under the headings Where You Can Find Information and Information Incorporated by Reference.

Cytokinetics, Incorporated

Cytokinetics, Incorporated is a leading biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule drugs that specifically target the cytoskeleton. A number of commonly used drugs and a growing body of research validate the role the cytoskeleton plays in a wide array of human diseases. Our focus on the cytoskeleton enables us to develop novel and potentially safer and more effective drugs for the treatment of these diseases. We believe that our cell biology driven approach and proprietary technologies enhance the speed, efficiency and yield of our drug discovery and development process. To date, our unique approach has produced two cancer drug candidates, a potential drug candidate for the treatment of congestive heart failure, and other research programs addressing a variety of other disease areas including high blood pressure and asthma.

We were incorporated in Delaware in August 1997. Our principal executive offices are located at 280 East Grand Avenue, South San Francisco, California 94080 and our telephone number at that address is (650) 624-3000.

CYTOKINETICS, our logo used alone and with the mark CYTOKINETICS, and CYTOMETRIX are our registered service marks and trademarks. Other service marks, trademarks and trade names referred to in this prospectus are the property of their respective owners.

Table of Contents

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the risks described below before making an investment decision. You should also refer to the other information in this prospectus, including our financial statements and the related notes incorporated by reference into this prospectus. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. If any of the following risks actually occur, our business, results of operations and financial condition could suffer. In that event, the trading price of the securities being offered by this prospectus could decline, and you may lose all or part of your investment in such securities. The risks discussed below also include forward-looking statements and our actual results may differ substantially from those discussed in these forward-looking statements.

Risks Related to Our Business

Our initial drug candidates are in the early stages of clinical testing and we have a history of significant losses and may not achieve or sustain profitability and, as a result, you may lose all or part of your investment.

Our initial drug candidates are in the early stages of clinical testing and we must conduct significant additional clinical trials before we can seek the regulatory approvals necessary to begin commercial sales of our drugs. We have incurred operating losses in each year since our inception in 1997 due to costs incurred in connection with our research and development activities and general and administrative costs associated with our operations. We expect to incur increasing losses for at least several years, as we continue our research activities and conduct development of, and seek regulatory approvals for, our initial drug candidates, and commercialize any approved drugs. If our initial drug candidates fail in clinical trials or do not gain regulatory approval, or if our drugs do not achieve market acceptance, we will not be profitable. If we fail to become and remain profitable, or if we are unable to fund our continuing losses, you could lose all or part of your investment.

We have never generated, and may never generate, revenues from commercial sales of our drugs and we may not have drugs to market for at least several years, if ever.

We currently have no drugs for sale and we cannot guarantee that we will ever have marketable drugs. We must demonstrate that our drug candidates satisfy rigorous standards of safety and efficacy to the Food and Drug Administration, or FDA, and other regulatory authorities in the United States and abroad. We and our partners will need to conduct significant additional research, preclinical testing and clinical testing, before we or our partners can file applications with the FDA or other regulatory authorities for approval of our drug candidates. In addition, to compete effectively, our drugs must be easy to use, cost-effective and economical to manufacture on a commercial scale. We may not achieve any of these objectives. Ispinesib, our most advanced drug candidate for the treatment of cancer, and SB-743921, our second drug candidate for the treatment of cancer, are currently our only drug candidates in clinical trials and we cannot be certain that the clinical development of these or any other drug candidate in preclinical testing or clinical development will be successful, that they will receive the regulatory approvals required to commercialize them, or that any of our other research programs will yield a drug candidate suitable for entry into clinical trials. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. The development of one or both of these drug candidates may be discontinued at any stage of our clinical trials programs and we may not generate revenue from either of these drug candidates.

Table of Contents

We have funded all of our operations and capital expenditures with proceeds from both private and public sales of our equity securities, strategic alliances with GlaxoSmithKline, or GSK, AstraZeneca and others, equipment financings, interest on investments and government grants. To meet our future cash requirements, we may raise funds through public or private equity offerings, debt financings or strategic alliances. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience additional dilution. To the extent that we raise additional funds through debt financing, if available, such financing may involve covenants that restrict our business activities. To the extent that we raise additional funds through strategic alliance and licensing arrangements, we will likely have to relinquish valuable rights to our technologies, research programs or drug candidates, or grant licenses on terms that may not be favorable to us. In addition, we cannot assure you that any such funding, if needed, will be available on attractive terms, or at all.

Clinical trials may fail to demonstrate the safety and efficacy of our drug candidates, which could prevent or significantly delay completion of clinical development and regulatory approval.

Prior to receiving approval to commercialize any of our drug candidates, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA and other regulatory authorities in the United States and abroad, that such drug candidate is both safe and effective. Before we can commence clinical trials, we must demonstrate through preclinical studies satisfactory product chemistry, formulation, stability and toxicity levels in order to file an investigational new drug application, or IND, (or the foreign equivalent of an IND) to commence clinical trials. In clinical trials we will need to demonstrate efficacy for the treatment of specific indications and monitor safety throughout the clinical development process. Long-term safety and efficacy have not yet been demonstrated in clinical trials for any of our drug candidates, and satisfactory chemistry, formulation, stability and toxicity levels have not yet been demonstrated for our drug candidates or compounds that are currently the subject of preclinical studies. If our preclinical studies, clinical trials or future clinical trials are unsuccessful, our business and reputation would be harmed and our stock price would be negatively affected.

All of our drug candidates are prone to the risks of failure inherent in drug development. Preclinical studies may not yield results that would satisfactorily support the filing of an IND or comparable regulatory filing abroad with respect to our drug candidates, and, even if these applications would be or have been filed with respect to our drug candidates, the results of preclinical studies do not necessarily predict the results of clinical trials. Similarly, early-stage clinical trials do not predict the results of later-stage clinical trials, including the safety and efficacy profiles of any particular drug candidate. In addition, there can be no assurance that the design of our clinical trials is focused on appropriate tumor types, patient populations, dosing regimens or other variables which will result in obtaining the desired efficacy data to support regulatory approval to commercialize the drug. Even if we believe the data collected from clinical trials of our drug candidates are promising, such data may not be sufficient to support approval by the FDA or any other United States or foreign regulatory authority. Preclinical and clinical data can be interpreted in different ways. Accordingly, FDA officials, or officials from foreign regulatory authorities, could interpret the data in different ways than we or our partners do, which could delay, limit or prevent regulatory approval.

Administering any of our drug candidates or potential drug candidates that are the subject of preclinical studies to animals may produce undesirable side effects, also known as adverse effects. Toxicities and adverse effects that we have observed in preclinical studies for some compounds in a particular research program may recur in preclinical studies of other compounds from the same program. Such toxicities or adverse effects could delay or prevent the filing of an IND or comparable regulatory filing abroad with respect to such drug candidates or potential drug candidates. In Phase I clinical trials of ispinesib, the dose limiting toxicity was neutropenia, a decrease in the number of a certain type of white blood cell that results in an increase in susceptibility to infection. In clinical trials, administering any of our drug candidates to

Table of Contents

humans may produce adverse effects. These adverse effects could interrupt, delay or halt clinical trials of our drug candidates and could result in the FDA or other regulatory authorities denying approval of our drug candidates for any or all targeted indications. The FDA, other regulatory authorities, our partners or we may suspend or terminate clinical trials at any time. Even if one or more of our drug candidates were approved for sale, the occurrence of even a limited number of toxicities or adverse effects when used in large populations may cause the FDA to impose restrictions on, or prevent, the further marketing of such drugs. Indications of potential adverse effects or toxicities which may occur in clinical trials and which we believe are not significant during the course of such trials may later turn out to actually constitute serious adverse effects or toxicities when a drug has been used in large populations or for extended periods of time. Any failure or significant delay in completing preclinical studies or clinical trials for our drug candidates, or in receiving and maintaining regulatory approval for the sale of any drugs resulting from our drug candidates, may severely harm our reputation and business.

Clinical trials are expensive, time consuming and subject to delay.

Clinical trials are very expensive and difficult to design and implement, especially in the cancer and congestive heart failure indications that we are pursuing, in part because they are subject to rigorous requirements. The clinical trial process is also time consuming. According to industry sources, the entire drug development and testing process takes on average 12 to 15 years. According to industry studies, the fully capitalized resource cost of new drug development averages approximately \$800 million, however, individual trials and individual drug candidates may incur a range of costs above or below this average. We estimate that clinical trials of our most advanced drug candidates will continue for several years, but may take significantly longer to complete. The commencement and completion of our clinical trials could be delayed or prevented by several factors, including, but not limited to:

delays in obtaining regulatory approvals to commence a study;

delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;

slower than expected rates of patient recruitment and enrollment, including as a result of the introduction of alternative therapies or drugs by others;

lack of effectiveness during clinical trials;

unforeseen safety issues;

uncertain dosing issues;

introduction of new therapies or changes in standards of practice or regulatory guidance that render our clinical trial endpoints or the targeting of our proposed indications obsolete;

inability to monitor patients adequately during or after treatment; and

inability or unwillingness of medical investigators to follow our clinical protocols.

We do not know whether planned clinical trials will begin on time, will need to be restructured or will be completed on schedule, if at all. Significant delays in clinical trials will impede our ability to commercialize our drug candidates and generate revenue and could significantly increase our development costs.

Table of Contents**We depend on GSK for the conduct, completion and funding of the clinical development and commercialization of our current drug candidates for the treatment of cancer.**

Under our strategic alliance with GSK, GSK is currently responsible for the clinical development and regulatory approval of our cancer drug candidates, ispinesib and SB-743921. GSK is responsible for filing applications with the FDA or other regulatory authorities for approval of these drug candidates, and will be the owner of any marketing approvals issued by the FDA or other regulatory authorities. If the FDA or other regulatory authorities approve these drug candidates, GSK will also be responsible for the marketing and sale of these drugs. Because GSK is responsible for these functions, we cannot control whether GSK will devote sufficient attention and resources to the clinical trials program or will proceed in an expeditious manner. Under certain circumstances, GSK has discretion to elect whether to pursue the development of our drug candidates or to abandon the clinical trial programs, and, after June 20, 2006, GSK may terminate our strategic alliance for any reason upon six months prior notice. These decisions are outside our control. Because both of our cancer drug candidates being developed by GSK act through inhibition of kinesin spindle protein, or KSP, a protein that is a member of a class of cytoskeletal proteins called mitotic kinesins that regulate DNA division, or mitosis, during cell division, it is possible that GSK may elect to proceed with the development of only one such drug candidate. If GSK were to elect to proceed with the development of SB-743921 in lieu of ispinesib, and because SB-743921 is at an earlier stage of clinical development than ispinesib, the approval, if any, of a new drug application, or NDA, with respect to a drug candidate from our cancer program would be delayed. In particular, if the initial clinical results of some of our early clinical trials do not meet GSK's expectations, GSK may elect to terminate further development of one or both drug candidates, even though the actual number of patients that have been treated is relatively small. Abandonment of one or both of ispinesib and SB-743921 by GSK would result in a delay in or prevent us from commercializing such drug candidates, and would delay or prevent our ability to generate revenues. Disputes may arise between us and GSK, which may delay or cause termination of the clinical trials program, result in significant litigation or arbitration, or cause GSK to act in a manner that is not in our best interest. If development of our drug candidates does not progress for these or any other reasons, we would not receive further milestone payments from GSK. GSK also has the contractual right to reduce its funding of our FTEs for this program at their discretion, subject to certain agreed minimum levels, in the beginning of each contract year based on the activities of the agreed upon research plan. Even if the FDA or other regulatory agencies approve one or more of our drug candidates, GSK may elect not to proceed with the commercialization of such drugs, or may elect to pursue commercialization of one drug but not others, and these decisions are outside our control. In such event, or in the event that GSK abandons development of any drug candidate prior to regulatory approval, we would have to undertake and fund the clinical development of our drug candidates or commercialization of our drugs, seek a new partner for clinical development or commercialization, or curtail or abandon the clinical development or commercialization programs. If we were unable to do so on acceptable terms, or at all, our business would be harmed, and the price of our common stock and other securities, if any, would be negatively affected.

If we fail to enter into and maintain successful strategic alliances for certain of our drug candidates, we may have to reduce or delay our drug candidate development or increase our expenditures.

Our strategy for developing, manufacturing and commercializing certain of our drug candidates currently requires us to enter into and successfully maintain strategic alliances with pharmaceutical companies or other industry participants to advance our programs and reduce our expenditures on each program. We have formed a strategic alliance with GSK with respect to ispinesib, SB-743921 and certain other research activities. However, we may not be able to negotiate additional strategic alliances on acceptable terms, if at all. If we are not able to maintain our existing strategic alliances or establish and maintain additional strategic alliances, we may have to limit the size or scope of, or delay, one or more of our drug development programs or research programs or undertake and fund these programs ourselves. If we elect to increase our

Table of Contents

expenditures to fund drug development programs or research programs on our own, we will need to obtain additional capital, which may not be available on acceptable terms, or at all.

The success of our development efforts depends in part on the performance of our partners and the National Cancer Institute, or NCI, over which we have little or no control.

Our ability to commercialize drugs that we develop with our partners and that generate royalties from product sales depends on our partners' abilities to assist us in establishing the safety and efficacy of our drug candidates, obtaining and maintaining regulatory approvals and achieving market acceptance of the drugs once commercialized. Our partners may elect to delay or terminate development of one or more drug candidates, independently develop drugs that could compete with ours or fail to commit sufficient resources to the marketing and distribution of drugs developed through their strategic alliances with us. It is likely that our partners will not proceed with the development and commercialization of our drug candidates with the same degree of urgency as we would because of other priorities they face. In particular, we are relying on the NCI to conduct several important clinical trials of our drug candidates. The NCI is a government agency and there can be no assurance that the NCI will not modify its plans to conduct such trials or will proceed with such trials diligently. If our partners fail to perform as we expect, our potential for revenue from drugs developed through our strategic alliances could be dramatically reduced.

Our focus on the discovery of drug candidates directed against specific proteins and pathways within the cytoskeleton is unproven, and we do not know whether we will be able to develop any drug candidates of commercial value.

We believe that our focus on drug discovery and development directed at the cytoskeleton is novel and unique to us. While a number of commonly used drugs and a growing body of research validate the importance of the cytoskeleton in the origin and progression of a number of diseases, no existing drugs specifically and directly interact with the cytoskeletal proteins and pathways that our drug candidates seek to modulate. As a result, we cannot be certain that our drug candidates will appropriately modulate targeted cytoskeletal proteins and pathways or produce commercially viable drugs that safely and effectively treat cancer, congestive heart failure or other diseases, or that the results we have seen in preclinical models will translate into similar results in humans. In addition, even if we are successful in developing and receiving regulatory approval for a commercially viable drug for the treatment of one disease focused on the cytoskeleton, we cannot be certain that we will also be able to develop and receive regulatory approval for drug candidates for the treatment of other forms of that disease or other diseases. If we or our partners fail to develop and commercialize viable drugs, we will not achieve commercial success.

Our proprietary rights may not adequately protect our technologies and drug candidates.

Our commercial success will depend in part on our obtaining and maintaining patent protection and trade secret protection of our technologies and drug candidates as well as successfully defending these patents against third-party challenges. We will only be able to protect our technologies and drug candidates from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them. Furthermore, the degree of future protection of 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.

The patent positions of life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in

Table of Contents

interpretations of patent laws in the United States or other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. For example:

we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents;

we or our licensors might not have been the first to file patent applications for these inventions;

others may independently develop similar or alternative technologies or duplicate any of our technologies;

it is possible that none of our pending patent applications or the pending patent applications of our licensors will result in issued patents;

our issued patents and issued patents of our licensors may not provide a basis for commercially viable drugs, or may not provide us with any competitive advantages, or may be challenged and invalidated by third parties;

we may not develop additional proprietary technologies or drug candidates that are patentable; or

We also rely on trade secrets to protect our technology, especially where we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our or our strategic partners' employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our information to competitors. If we were to enforce a claim that a third party had illegally obtained and was using our trade secrets, our enforcement efforts would be expensive and time consuming, and the outcome would be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, if our competitors independently develop equivalent knowledge, methods and know-how, it will be more difficult for us to enforce our rights and our business could be harmed.

If we are not able to defend the patent or trade secret protection position of our technologies and drug candidates, then we will not be able to exclude competitors from developing or marketing competing drugs, and we may not generate enough revenue from product sales to justify the cost of development of our drugs and to achieve or maintain profitability.

If we are sued for infringing intellectual property rights of third parties, such litigation will be costly and time consuming, and an unfavorable outcome would have a significant adverse effect on our business.

Our ability to commercialize drugs depends on our ability to sell such drugs without infringing the patents or other proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the areas that we are exploring. In addition, because patent applications can take several years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our drug candidates may infringe. There could also be existing patents of which we are not aware that our drug candidates may inadvertently infringe.

In particular, we are aware of an issued U.S. patent and at least one pending U.S. patent application assigned to Curis, Inc. relating to certain compounds in the quinazolinone class. Ispinesib falls into this class of compounds. The Curis patent claims a method of use for inhibiting signaling by what is called the

Table of Contents

hedgehog pathway using certain such compounds. Curis has pending applications in Europe, Japan, Australia and Canada with claims covering compositions of certain quinazolinone compounds. We are also aware that the Australian application and one of the European applications have been granted. In addition, in Europe, Australia and elsewhere, the grant of a patent may be opposed by one or more parties. Curis or a third party may assert that the sale of ispinosib may infringe one or more of these or other patents. We believe that we have valid defenses against the Curis patents if asserted against us. However, we cannot guarantee that a court would find such defenses valid or that such oppositions would be successful. We have not attempted to obtain a license to this patent. If we decide to obtain a license to this patent, we cannot guarantee that we would be able to obtain such a license on commercially reasonable terms, or at all.

In addition, we are aware of various issued U.S. patents and pending U.S. and foreign patent applications assigned to Cellomics, Inc. relating to an automated method for analyzing cells. One of these applications was granted in Europe. Cellomics or a third party may assert that our Cytometrix technologies fall within the scope of, and thus infringe, one or more of these patents. We have received a letter from Cellomics notifying us that Cellomics believes we may be practicing one or more of their patents and that Cellomics offers a use license for such patents through its licensing program. We believe that we have valid defenses to such an assertion. Moreover, the grant of the European patent may be opposed by one or more parties. However, we cannot guarantee that a court would find such defenses valid or that such opposition would be successful. If we decide to obtain a license to these patents, we cannot guarantee that we would be able to obtain such a license on commercially reasonable terms, or at all.

Other future products of ours may be impacted by patents of companies engaged in competitive programs with significantly greater resources (such as Merck & Co., Inc., or Merck). Further development of these products could be impacted by these patents and result in the expenditure of significant legal fees.

If a third party claims that we infringe on their patents or other proprietary rights, we could face a number of issues that could seriously harm our competitive position, including, but not limited to:

infringement and other intellectual property claims that, with or without merit, can be costly and time consuming to litigate and can delay the regulatory approval process and divert management's attention from our core business strategy;

substantial damages for past infringement which we may have to pay if a court determines that our drugs or technologies infringe upon a competitor's patent or other proprietary rights;

a court prohibiting us from selling or licensing our drugs or technologies unless the holder licenses the patent or other proprietary rights to us, which it is not required to do; and

if a license is available from a holder, we may have to pay substantial royalties or grant cross licenses to our patents or other proprietary rights.

We may become involved in disputes with our strategic partners over intellectual property ownership, and publications by our research collaborators and scientific advisors could impair our ability to obtain patent protection or protect our proprietary information, which, in either case, would have a significant impact on our business.

Inventions discovered under our strategic alliance agreements become jointly owned by our strategic partners and us in some cases, and the exclusive property of one of us in other cases. Under some circumstances, it may be difficult to determine who owns a particular invention, or whether it is jointly owned, and disputes could arise regarding ownership of those inventions. These disputes could be costly and

Table of Contents

time consuming, and an unfavorable outcome would have a significant adverse effect on our business if we were not able to protect or license rights to these inventions. In addition, our research collaborators and scientific advisors have contractual rights to publish our data and other proprietary information, subject to our prior review. Publications by our research collaborators and scientific advisors containing such information, either with our permission or in contravention of the terms of their agreements with us, may impair our ability to obtain patent protection or protect our proprietary information, which could significantly harm our business.

To the extent we elect to fund the development of a drug candidate or the commercialization of a drug at our expense, we will need substantial additional funding.

The discovery, development and commercialization of novel small molecule drugs focused on the cytoskeleton for the treatment of a wide array of diseases is costly. As a result, to the extent we elect to fund the development of a drug candidate or the commercialization of a drug at our expense, we will need to raise additional capital to:

- expand our research and development and technologies;
- fund clinical trials and seek regulatory approvals;
- build or access manufacturing and commercialization capabilities;
- implement additional internal systems and infrastructure;
- maintain, defend and expand the scope of our intellectual property; and
- hire and support additional management and scientific personnel.

Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and cost of our clinical trials and other research and development activities;
- the costs and timing of seeking and obtaining regulatory approvals;
- the costs associated with establishing manufacturing and commercialization capabilities;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs of acquiring or investing in businesses, products and technologies;
- the effect of competing technological and market developments; and
- the payment and other terms and timing of any strategic alliance, licensing or other arrangements that we may establish.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs primarily through public or private equity offerings, debt financings or strategic alliances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are not able to secure additional funding when needed, we may have to

Table of Contents

delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or future commercialization initiatives.

We have no capacity to carry out our own clinical trials in connection with the development of our drug candidates and potential drug candidates, and to the extent we elect to develop a drug candidate without a strategic partner we will need to develop such capacity, and we will require additional funding.

The development of drug candidates is complicated, and requires resources and experience that we do not have. Currently, we rely on our strategic partners to carry out these activities for those of our drug candidates that are in clinical trials. However, we do not have a partner for our potential cardiac myosin activator drug candidate, or, in the event GSK elects to terminate its development efforts, an alternative partner for our cancer drug candidates. To the extent we decide to initiate clinical trials for a drug candidate without support from a strategic partner, such as a potential drug candidate from our cardiovascular disease program, we will need to develop the skills, technical expertise and resources necessary to carry out such development efforts on our own or through the use of other third parties, such as contract research organizations, or CROs.

If we utilize CROs, we will not have control over many aspects of their activities, and will not be able to control the amount or timing of resources that they devote to our programs. These third parties also may not assign as high a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves, and therefore may not complete their respective activities on schedule. CROs may also have relationships with our competitors and potential competitors, and may prioritize those relationships ahead of their relationships with us. Typically, we would have to qualify more than one vendor for each function performed outside of our control, which could be time consuming and costly. The failure of CROs to carry out development efforts on our behalf according to our requirements and FDA or other regulatory agencies' standards, or our failure to properly coordinate and manage such efforts, could increase the cost of our operations and delay or prevent the development, approval and commercialization of our drug candidates.

If we fail to develop the skills, technical expertise and resources necessary to carry out the development of our drug candidates, or if we fail to effectively manage our CROs carrying out such development, the commercialization of our drug candidates will be delayed or prevented.

We currently have no marketing or sales staff, and if we are unable to enter into or maintain strategic alliances with marketing partners or if we are unable to develop our own sales and marketing capabilities, we may not be successful in commercializing our potential drugs.

We currently have no sales, marketing or distribution capabilities. To commercialize our drugs that we determine not to market on our own, we will depend on strategic alliances with third parties, such as GSK, which have established distribution systems and direct sales forces. If we are unable to enter into such arrangements on acceptable terms, we may not be able to successfully commercialize such drugs.

We plan to commercialize drugs on our own, with or without a partner, that can be effectively marketed and sold in concentrated markets that do not require a large sales force to be competitive. To achieve this goal, we will need to establish our own specialized sales force and marketing organization with technical expertise and with supporting distribution capabilities. Developing such an organization is expensive and time consuming and could delay a product launch. In addition, we may not be able to develop this capacity efficiently, or at all, which could make us unable to commercialize our drugs.

Table of Contents

To the extent that we are not successful in commercializing any drugs ourselves or through a strategic alliance, our product revenues will suffer, we will incur significant additional losses and the price of our common stock and other securities, if any, will be negatively affected.

We have no manufacturing capacity, depend on a single contract manufacturer to produce our clinical trial drug supplies, and anticipate continued reliance on contract manufacturers for the development and commercialization of our potential drugs.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates under development. We have no experience in drug formulation or manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale. As a result, we currently rely on a single contract manufacturer to supply, store and distribute drug supplies for our clinical trials and anticipate future reliance on a limited number of contract manufacturers until we are able to expand our operations to include manufacturing capacities. Any performance failure on the part of our existing or future contract manufacturers could delay clinical development or regulatory approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential product revenues.

Our drug candidates require precise, high quality manufacturing. Our failure or our contract manufacturer's failure to achieve and maintain high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business. Contract drug manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. These manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the United States Drug Enforcement Agency and other regulatory agencies to ensure strict compliance with current good manufacturing practices and other applicable government regulations and corresponding foreign standards; however, we do not have control over contract manufacturers' compliance with these regulations and standards. If one of our contract manufacturers fails to maintain compliance, the production of our drug candidates could be interrupted, resulting in delays, additional costs and potentially lost revenues. Additionally, our contract manufacturer must pass a preapproval inspection before we can obtain marketing approval for any of our drug candidates in development.

If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, we will need to manufacture them in larger quantities. To date, our drug candidates have been manufactured in small quantities for preclinical testing and clinical trials and we may not be able to successfully increase the manufacturing capacity, whether in collaboration with contract manufacturers or on our own, for any of our drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we are unable to successfully increase the manufacturing capacity for a drug candidate, the regulatory approval or commercial launch of any related drugs may be delayed or there may be a shortage in supply. Even if any contract manufacturer makes improvements in the manufacturing process for our drug candidates, we may not own, or may have to share, the intellectual property rights to such improvements.

In addition, our existing and future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our drug candidates. We currently rely on a single contract manufacturer as the sole supply source for our drug candidates. In the event of a natural disaster, business failure, strike or other difficulty, we may be unable to replace such contract manufacturer in a timely manner and the production of our drug candidates would be interrupted, resulting in delays and additional costs.

Table of Contents

Switching manufacturers may be difficult because the number of potential manufacturers is limited and the FDA must approve any replacement manufacturer prior to manufacturing our drug candidates. Such approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our drug candidates after receipt of FDA approval. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all.

We expect to expand our development, clinical research and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to have significant growth in expenditures, the number of our employees and the scope of our operations, in particular with respect to those drug candidates that we elect to develop or commercialize independently or together with a partner. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

The failure to attract and retain skilled personnel could impair our drug development and commercialization efforts.

Our performance is substantially dependent on the performance of our senior management and key scientific and technical personnel, particularly James H. Sabry, M.D., Ph.D., our President and Chief Executive Officer, Robert I. Blum, our Executive Vice President, Corporate Development and Commercial Operations and Chief Business Officer, Andrew A. Wolff, M.D., F.A.C.C., our Senior Vice President, Clinical Research and Chief Medical Officer, and Sharon A. Surrey-Barbari, our Senior Vice President, Finance and Chief Financial Officer. The employment of these individuals and our other personnel is terminable at will with short or no notice. We carry key person life insurance on James H. Sabry, M.D., Ph.D. The loss of the services of any member of our senior management, scientific or technical staff may significantly delay or prevent the achievement of drug development and other business objectives by diverting management's attention to transition matters and identification of suitable replacements, and could have a material adverse effect on our business, operating results and financial condition. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us.

In addition, we believe that we will need to recruit additional executive management and scientific and technical personnel. There is currently intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. Our inability to attract and retain sufficient scientific, technical and managerial personnel could limit or delay our product development efforts, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

Table of Contents

Risks Related to Our Industry

Our competitors may develop drugs that are less expensive, safer, or more effective, which may diminish or eliminate the commercial success of any drugs that we may commercialize.

We compete with companies that are also developing drug candidates that focus on the cytoskeleton, as well as companies that have developed drugs or are developing alternative drug candidates for cancer and cardiovascular, infectious and other diseases. For example, with respect to cancer, Bristol-Myers Squibb's Taxol® (paclitaxel), Sanofi Aventis Pharmaceuticals Inc.'s Taxotere® (docetaxel), and generic equivalents of Taxol are currently available on the market and commonly used in cancer treatment. Furthermore, we are aware that Merck, Chiron Corp., Bristol-Myers Squibb and other pharmaceutical and biopharmaceutical companies are conducting research focused on KSP and other mitotic kinesins. In addition, Bristol-Myers Squibb, Merck, Novartis and other pharmaceutical and biopharmaceutical companies are developing other approaches to inhibiting mitosis. With respect to congestive heart failure, we are aware of a potentially competitive approach being developed by Orion in collaboration with Abbott Laboratories.

Our competitors may:

develop drug candidates and market drugs that are less expensive or more effective than our future drugs;

commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates;

obtain proprietary rights that could prevent us from commercializing our products;

initiate or withstand substantial price competition more successfully than we can;

have greater success in recruiting skilled scientific workers from the limited pool of available talent;

more effectively negotiate third-party licenses and strategic alliances;

take advantage of acquisition or other opportunities more readily than we can;

develop drug candidates and market drugs that increase the levels of efficacy or alter other drug candidate profile aspects that our drug candidates need to show in order to obtain regulatory approval; and

introduce therapies or market drugs that render the market opportunity for our potential drugs obsolete.

We will compete for market share against large pharmaceutical and biotechnology companies and smaller companies that are collaborating with larger pharmaceutical companies, new companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors, either alone or together with their partners, may develop new drug candidates that will compete with ours, as these competitors may, and in certain cases do, operate larger research and development programs or have substantially greater financial resources than we do. Our competitors may also have significantly greater experience in:

Table of Contents

developing drug candidates;

undertaking preclinical testing and clinical trials;

building relationships with key customers and opinion-leading physicians;

obtaining and maintaining FDA and other regulatory approvals of drug candidates;

formulating and manufacturing drugs; and

launching, marketing and selling drugs.

If our competitors market drugs that are less expensive, safer or more effective than our potential drugs, or that reach the market sooner than our potential drugs, we may not achieve commercial success. In addition, the life sciences industry is characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change we may be unable to compete effectively. Our competitors may render our technologies obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies.

The regulatory approval process is expensive, time consuming and uncertain and may prevent our partners or us from obtaining approvals for the commercialization of some or all of our drug candidates.

The research, testing, manufacturing, selling and marketing of drug candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. Neither we nor our partners are permitted to market our potential drugs in the United States until we receive approval of a new drug application, or NDA, from the FDA. Neither we nor our partners have received marketing approval for any of our drug candidates. Obtaining an NDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with the FDA and other applicable foreign and United States regulatory requirements may subject us to administrative or judicially imposed sanctions. These include warning letters, civil and criminal penalties, injunctions, product seizure or detention, product recalls, total or partial suspension of production, and refusal to approve pending NDAs, or supplements to approved NDAs.

Regulatory approval of an NDA or NDA supplement is never guaranteed, and the approval process typically takes several years and is extremely expensive. The FDA also has substantial discretion in the drug approval process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon clinical trials or to repeat or perform additional preclinical testing and clinical trials. The number and focus of preclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. The FDA can delay, limit or deny approval of a drug candidate for many reasons, including:

a drug candidate may not be safe or effective;

FDA officials may not find the data from preclinical testing and clinical trials sufficient;

the FDA might not approve our or our contract manufacturer's processes or facilities; or

Table of Contents

the FDA may change its approval policies or adopt new regulations.

If we or our partners receive regulatory approval for our drug candidates, we will also be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we may also be subject to additional FDA post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize our potential drugs.

Any regulatory approvals that we or our partners receive for our drug candidates may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for potentially costly post-marketing follow-up studies. In addition, if the FDA approves any of our drug candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business could suffer.

If physicians and patients do not accept our drugs, we may be unable to generate significant revenue, if any.

Even if our drug candidates obtain regulatory approval, resulting drugs, if any, may not gain market acceptance among physicians, healthcare payors, patients and the medical community. Even if the clinical safety and efficacy of drugs developed from our drug candidates are established for purposes of approval, physicians may elect not to recommend these drugs for a variety of reasons including, but not limited to:

timing of market introduction of competitive drugs;

clinical safety and efficacy of alternative drugs or treatments;

cost-effectiveness;

availability of reimbursement from health maintenance organizations and other third-party payors;

convenience and ease of administration;

prevalence and severity of adverse side effects;

other potential disadvantages relative to alternative treatment methods; and

insufficient marketing and distribution support.

If our drugs fail to achieve market acceptance, we may not be able to generate significant revenue and our business would suffer.

Table of Contents

The coverage and reimbursement status of newly approved drugs is uncertain and failure to obtain adequate coverage and reimbursement could limit our ability to market any drugs we may develop and decrease our ability to generate revenue.

There is significant uncertainty related to the coverage and reimbursement of newly approved drugs. The commercial success of our potential drugs in both domestic and international markets is substantially dependent on whether third-party coverage and reimbursement is available for the ordering of our potential drugs by the medical profession for use by their patients. Medicare, Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs, and, as a result, they may not cover or provide adequate payment for our potential drugs. They may not view our potential drugs as cost-effective and reimbursement may not be available to consumers or may not be sufficient to allow our potential drugs to be marketed on a competitive basis. Likewise, legislative or regulatory efforts to control or reduce healthcare costs or reform government healthcare programs could result in lower prices or rejection of coverage for our potential drugs. Changes in coverage and reimbursement policies or healthcare cost containment initiatives that limit or restrict reimbursement for our drugs may cause our revenue to decline.

We may be subject to costly product liability claims and may not be able to obtain adequate insurance.

Because we conduct clinical trials in humans, we face the risk that the use of our drug candidates will result in adverse effects. We currently maintain product liability insurance in the amount of \$10.0 million with a \$5,000 deductible per occurrence, however, such liability insurance currently excludes coverage of liability resulting from clinical trials. We cannot predict the possible harms or side effects that may result from our clinical trials. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limit of, our insurance coverage.

In addition, once we have commercially launched drugs based on our drug candidates, we will face exposure to product liability claims. This risk exists even with respect to those drugs that are approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA. We intend to secure limited product liability insurance coverage, but may not be able to obtain such insurance on acceptable terms with adequate coverage, or at reasonable costs. There is also a risk that third parties that we have agreed to indemnify could incur liability. Even if we were ultimately successful in product liability litigation, the litigation would consume substantial amounts of our financial and managerial resources and may create adverse publicity, all of which would impair our ability to generate sales of the affected product as well as our other potential drugs. Moreover, product recalls may be issued at our discretion or at the direction of the FDA, other governmental agencies or other companies having regulatory control for drug sales. If product recalls occur, such recalls are generally expensive and often have an adverse effect on the image of the drugs being recalled as well as the reputation of the drug's developer or manufacturer.

We may be subject to damages resulting from claims that our employees or we have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or prevent our ability to commercialize certain

Table of Contents

potential drugs, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

We use hazardous chemicals and radioactive and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from those materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

In addition, our partners may use hazardous materials in connection with our strategic alliances. To our knowledge, their work is performed in accordance with applicable biosafety regulations. In the event of a lawsuit or investigation, however, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials used by these parties. Further, we may be required to indemnify our partners against all damages and other liabilities arising out of our development activities or drugs produced in connection with these strategic alliances.

Our facilities in California are located near an earthquake fault, and an earthquake or other types of natural disasters or resource shortages could disrupt our operations and adversely affect results.

Important documents and records, such as hard copies of our laboratory books and records for our drug candidates and compounds, are located in our corporate headquarters at a single location in South San Francisco, California near active earthquake zones. In the event of a natural disaster, such as an earthquake, drought or flood, or localized extended outages of critical utilities or transportation systems, we do not have a formal business continuity or disaster recovery plan, and could therefore experience a significant business interruption. In addition, California from time to time has experienced shortages of water, electric power and natural gas. Future shortages and conservation measures could disrupt our operations and cause expense, thus adversely affecting our business and financial results.

Risks Related To an Investment in Our Securities

We expect that our stock price will fluctuate significantly, and you may not be able to resell your shares at or above your investment price.

The stock market, particularly in recent years, has experienced significant volatility particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. Factors that could cause this volatility in the market price of our common stock include, but are not limited to:

results from, and any delays in, the clinical trials programs for our drug candidates for the treatment of cancer, including the clinical trials for ispinosib and SB-743921, and including delays resulting from slower than expected patient enrollment in such trials;

Table of Contents

delays in or discontinuation of the development of any of our drug candidates by GSK;

failure or delays in entering additional drug candidates into clinical trials, including a potential drug candidate for the treatment of congestive heart failure;

failure or discontinuation of any of our research programs;

delays or other developments in establishing new strategic alliances;

announcements concerning our strategic alliances with GSK or AstraZeneca or future strategic alliances;

issuance of new or changed securities analysts' reports or recommendations;

market conditions in the pharmaceutical and biotechnology sectors;

actual or anticipated fluctuations in our quarterly financial and operating results;

developments or disputes concerning our intellectual property or other proprietary rights;

introduction of technological innovations or new commercial products by us or our competitors;

issues in manufacturing our drug candidates or drugs;

market acceptance of our drugs;

third-party healthcare reimbursement policies;

FDA or other United States or foreign regulatory actions affecting us or our industry;