CYTOKINETICS INC
Form 424B2
December 07, 2006

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The information in this prospectus supplement is not complete and may be changed. This prospectus supplement and accompanying prospectus are not offers to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer and sale is not permitted.

SUBJECT TO COMPLETION, DATED DECEMBER 6, 2006

To be filed pursuant to Rule 424(b)(2)
Registration Number 333-125786

Prospectus Supplement
(To Prospectus dated June 14, 2005)

Shares

Cytokinetics, Incorporated

Common Stock

Cytokinetics, Incorporated is offering up to shares of its common stock by this prospectus supplement at a price per share of $.

The common stock is quoted on the Nasdaq Global Market under the symbol CYTK. The last reported sale price of the common stock on December 6, 2006 was $7.46 per share.

We are offering these shares of common stock on a best efforts basis primarily to institutional investors. We have retained Lazard Capital Markets LLC, JMP Securities LLC and Rodman & Renshaw, LLC to act as co-placement agents in connection with this offering.

See Risk Factors on page S-3 of this prospectus supplement and on page 2 of the accompanying prospectus to read about factors you should consider before buying shares of the common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$	$
Placement Agents Fee	$	$
Proceeds, before expenses, to us	$	$

We estimate the total expenses of this offering, excluding the placement agents fee, will be approximately $. Because there is no minimum offering amount required as a condition to closing in this offering, the actual offering amount, the placement agents fee and net proceeds to us, if any, in this offering may be substantially less than the total maximum offering amounts set forth above. We are not required to sell any specific number or dollar amount of the shares of common stock offered in this offering, but the placement agents will use their best efforts to arrange for the sale of all of the shares of common stock offered. Pursuant to an escrow agreement among us, the placement agents and an escrow agent, some or all of the funds received in payment for the shares of common stock sold in this offering will be wired to an interest bearing escrow account and held until we and the placement agents notify the escrow agent that this offering has closed, indicating the date on which the shares of common stock are to be delivered to the purchasers and the proceeds are to be delivered to us.

Lazard Capital Markets

JMP Securities

Rodman & Renshaw

Prospectus Supplement dated December , 2006.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock being offered by us. The second part, the accompanying prospectus dated June 14, 2005, gives more general information about our common stock. You should read the entire prospectus supplement and the accompanying prospectus, as well as the information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. Under no circumstances should the delivery to you of this prospectus supplement and the accompanying prospectus or any sale made pursuant to this prospectus supplement create any implication that the information contained in this prospectus supplement and the accompanying prospectus is correct as of any time after the date of this prospectus supplement.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and/or the accompanying prospectus must inform themselves about, and

observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus supplement and the accompanying prospectus dated June 14, 2005 are part of a registration statement on Form S-3 (File No. 333-125786) we filed with the Securities and Exchange Commission using a shelf registration process. On October 30, 2006, we registered additional shares of common stock pursuant to Rule 462(b) of the Securities Act of 1933 on a registration statement on Form S-3 (File No. 333-138306). Under this shelf registration process, and as of October 30, 2006, we may from time to time sell any combination of securities described in the accompanying prospectus in one or more offerings up to a total of $80,400,000.

Unless we indicate otherwise, references in this prospectus supplement to Cytokinetics, we, our and us refer to Cytokinetics, Incorporated.

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THE OFFERING

Common Stock we are offering	shares
Common stock to be outstanding after this offering	shares
Risk factors	See Risk Factors beginning on page S-3 for a discussion of factors that you should consider before buying shares of our common stock.
Nasdaq Global Market Symbol	CYTK
Use of Proceeds	We intend to use the net proceeds of this offering to fund research and development, including clinical trials of our product candidates, and for general corporate purposes. See Use of Proceeds on page S-23 of this prospectus supplement.

The number of shares of common stock outstanding after this offering is based on the number of shares outstanding as of September 30, 2006. As of that date, we had 37,793,573 shares of common stock outstanding, excluding:

- 4,183,980 shares of our common stock issuable upon exercise of outstanding options granted under our stock option plans at a weighted average exercise price of $5.26 per share;
- 244,000 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average price of $9.13 per share; and
- 2,394,699 shares of common stock reserved for future awards under our stock option plans and our employee stock purchase plan.

See Description of Common Stock on page S-24 for additional information on the number of shares of common stock to be outstanding after this offering.

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RISK FACTORS

Our business is subject to various risks, including those described below. You should carefully consider the following risks, together with all of the other information included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference before investing in our common stock. Any of these risks could materially adversely affect our business, operating results and financial condition.

Risks Related To Our Business

Our 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 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 drug candidates, and commercialize any approved drugs. If our 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 U.S. 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 and preclinical 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, compared to other therapies available for the treatment of the same conditions. We may not achieve any of these objectives. Ispinesib, our most advanced drug candidate for the treatment of cancer, SB-743921, our second drug candidate for the treatment of cancer, and CK-1827452 in both intravenous and oral formulations, our drug candidates for the treatment of heart failure, 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 any one or all of these drug candidates may be discontinued at any stage of our clinical trials programs and we may not generate revenue from any of these drug candidates.

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We currently finance and plan to continue to finance our operations through the sale of equity and potentially entering into additional strategic alliances, which may result in additional dilution to our stockholders or relinquishment of valuable technology rights, or may cease to be available on attractive terms or at all.

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. We believe that our existing cash and cash equivalents, future payments from GSK, interest earned on investments, proceeds from equipment financings and potential proceeds from our committed equity financing facility, or CEFF, with Kingsbridge Capital Ltd., or Kingsbridge, will be sufficient to meet our projected operating requirements for at least the next 12 months. To meet our future cash requirements, we may raise funds through public or private equity offerings 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 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. To the extent that we raise additional funds through debt financing, if available, such financing may involve covenants that restrict our business activities. 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 desired 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 sufficiently safe and effective. In clinical trials we will need to demonstrate efficacy for the treatment of specific indications and monitor safety throughout the clinical development process. None of our drug candidates have yet demonstrated long-term safety and efficacy in clinical trials. In addition, for each of our current preclinical compounds, we must demonstrate satisfactory chemistry, formulation, stability and toxicity in order to file an investigational new drug application, or IND, or a foreign equivalent, that would allow us to advance that compound into clinical trials. If our preclinical studies, current clinical trials or future clinical trials are unsuccessful, our business and reputation will be harmed and our stock price will 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 a foreign equivalent) with respect to our potential 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 U.S. 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.

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Toxicities and adverse effects that we have observed in preclinical studies for some compounds in a particular research and development program may occur in preclinical studies or clinical trials of other compounds from the same program. Potential toxicity issues may arise from the effects of the active pharmaceutical ingredient, or API, itself or from impurities or degradants that are present in the API or could form over time in the formulated drug candidate or the API. Such toxicities or adverse effects could delay or prevent the filing of an IND (or a foreign equivalent) with respect to such drug candidates or potential drug candidates or cause us to cease clinical trials with respect to any drug candidate. In clinical trials, administering any of our drug candidates to humans may produce adverse effects. In 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 a Phase I clinical trial of SB-743921, the dose-limiting toxicities observed were: prolonged neutropenia, with or without fever and with or without infection; elevated transaminases and hyperbilirubinemia, both of which are abnormalities of liver function; and hyponatremia, which is a low concentration of sodium in the blood. In a Phase I clinical trial of CK-1827452, doses that exceeded the maximum tolerated dose of CK-1827452 were associated with increases in heart rate and declines in blood pressure. 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 stop, 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 clinical 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 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 studies, the entire drug development and testing process takes on average 12 to 15 years, and the fully capitalized resource cost of new drug development averages approximately $800 million. However, individual clinical trials and individual drug candidates may incur a range of costs or time demands above or below this average. We estimate that clinical trials of our most advanced drug candidates will continue for several years, but they may take significantly longer to complete. The commencement and completion of our clinical trials could be delayed or prevented by many factors, including, but not limited to:

- delays in obtaining regulatory or other approvals to commence and conduct a clinical trial;
- 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;
- inadequate supply of clinical trial material;

uncertain dosing issues;

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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, or whether planned or currently ongoing clinical trials 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.

We have limited 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 expand our development capacity, and will require additional funding.

The development of drug candidates is complicated, and the required resources and experience that we currently have to carry out such development are limited. Pursuant to our amended Collaboration and License Agreement with GSK, we are now responsible for conducting clinical development for our drug candidates ispinesib and SB-743921. Currently, we rely on GSK to conduct pre-clinical and clinical development for GSK-923295 and the National Cancer Institute, or NCI, to conduct certain clinical trials for ispinesib. We cannot engage a strategic partner for ispinesib or SB-743921 until GSK elects not to exercise its option to conduct clinical development for that drug candidate or its option expires. If GSK elects to terminate its development efforts with respect to GSK-923295, or not to exercise its option to conduct clinical development for either of ispinesib or SB-743921, we do not have an alternative strategic partner for these programs. We do not have a strategic partner for our cardiac myosin activator drug candidate, CK-1827452. For our drug candidates for which we expect to conduct clinical trials, such as ispinesib, SB-743921 and CK-1827452, we plan to rely on contractors for the manufacture and distribution of clinical supplies. To the extent we conduct clinical trials for a drug candidate without support from a strategic partner, we will need to develop additional 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 fully 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 prefer 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 and in accordance with applicable laws, 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. In addition, if a CRO fails to perform as agreed, our ability to collect damages may be contractually limited.

If we fail to develop the additional 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.

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We have no manufacturing capacity and depend on our strategic partners or contract manufacturers to produce our clinical trial drug supplies for each of our drug candidates and potential drug candidates, 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 or potential drug candidates. We have limited experience in drug formulation and 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 will rely on GSK to be responsible for such activities for the planned GSK-923295 clinical trial. For ispinesib, SB-743921, CK-1827452 and any future drug candidates for which we conduct clinical development, we expect to rely on a limited number of contract manufacturers, and, in particular, we expect to rely on single-source contract manufacturers for the active pharmaceutical ingredient and the drug product supply for our clinical trials. We anticipate continued reliance on a limited number of contract manufacturers. If any of our existing or future contract manufacturers fail to perform as agreed, it 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. In addition, if a contract manufacturer fails to perform as agreed, our ability to collect damages may be contractually limited.

Our drug candidates require precise, high quality manufacturing. The 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 stringent regulatory requirements, including the FDA s current good manufacturing practices regulations and similar foreign laws, as well as ongoing periodic unannounced inspections by the FDA, the U.S. 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 our 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 only in small quantities for preclinical testing and clinical trials. 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. If a natural disaster, business failure, strike or other difficulty occurs, 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.

Switching manufacturers or manufacturing sites may be difficult and time consuming because the number of potential manufacturers is limited. In addition, prior to the commercialization of a drug

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from any replacement manufacturer or manufacturing site, the FDA must approve that site. Such approval would require new testing and compliance inspections. In addition, a new manufacturer or manufacturing site would have to be educated in, or develop substantially equivalent processes for, production of our drugs 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 may not be able to successfully scale-up manufacture of our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing resulting approved drugs, if any.

To date, our drug candidates have been manufactured in small quantities for preclinical studies and early-stage clinical trials. In order to conduct larger scale or late-stage clinical trials for a drug candidate and for the resulting drug if that drug candidate is approved for sale, we will need to manufacture it in larger quantities. We may not be able to successfully increase the manufacturing capacity for any of our drug candidates, whether in collaboration with third-party manufacturers or on our own, in a timely or cost-effective manner or at all. Significant scale-up of manufacturing may require additional validation studies, which are costly and which the FDA must review and approve. In addition, quality issues may arise during such scale-up activities because of the inherent properties of a drug candidate itself or of a drug candidate in combination with other components added during the manufacturing and packaging process. If we are unable to successfully scale-up manufacture of any of our drug candidates in sufficient quality and quantity, the development, regulatory approval or commercial launch of that drug candidate may be delayed or there may be a shortage in supply, which could significantly harm our business.

We depend on GSK for the conduct, completion and funding of the clinical development and commercialization of GSK-923295.

Under our strategic alliance with GSK, as amended, GSK is responsible for the clinical development and regulatory approval of our potential drug candidate GSK-923295 for cancer and other indications. GSK is responsible for filing applications with the FDA or other regulatory authorities for approval of GSK-923295 and will be the owner of any marketing approvals issued by the FDA or other regulatory authorities for GSK-923295. If the FDA or other regulatory authorities approve GSK-923295, GSK will also be responsible for the marketing and sale of the resulting drug. Because GSK is responsible for these functions, we cannot control whether GSK will devote sufficient attention and resources to the clinical trials program for GSK-923295 or will proceed in an expeditious manner. GSK generally has discretion to elect whether to pursue or abandon the development of GSK-923295 and may terminate our strategic alliance for any reason upon six months prior notice. These decisions are outside our control.

In particular, if the initial clinical results of some of its early clinical trials do not meet GSK s expectations, GSK may elect to terminate further development of GSK-923295 or certain of the potential clinical trials for GSK-923295, even if the actual number of patients treated at such time is relatively small. If GSK abandons GSK-923295, it would result in a delay in or prevent us from commercializing GSK-923295, and would delay or prevent our ability to generate revenues. Disputes may arise between us and GSK, which may delay or cause the termination of any GSK-923295 clinical trials, result in significant litigation or arbitration, or cause GSK to act in a manner that is not in our best interest. If development of GSK-923295 does not progress for these or any other reasons, we would not receive further milestone payments from GSK with respect to GSK-923295. Even if the FDA or other regulatory agencies approve GSK-923295, GSK may elect not to proceed with the commercialization of the resulting drug. These decisions are outside our control. In such event, or if GSK abandons development of GSK-923295 prior to regulatory approval, we would have to undertake and fund the clinical development of GSK-923295 or commercialization of the resulting drug, seek a new partner for clinical development or commercialization, or curtail or abandon such clinical

development or commercialization. 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 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. 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 expenditures to fund drug development programs or research programs on our own, as we have under the amendment to our Collaboration and License Agreement with GSK through which we will be responsible for the clinical development of ispinesib and SB-743921, 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 GSK and the 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. Our partners may 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, a government agency, to conduct several clinical trials of ispinesib and GSK to conduct clinical development of GSK-923295. There can be no assurance that GSK or the NCI, or both, will not modify their respective plans to conduct such clinical development or will proceed with such clinical development diligently. We have no control over the conduct of clinical development being conducted by GSK or the NCI, including the timing of initiation, termination or completion of such clinical trials, the analysis of data arising out of such clinical trials or the timing of release of complete data concerning such clinical trials, which may impact our ability to report on their results. If our partners fail to perform as we expect, our potential for revenue from drugs developed through our strategic alliances, if any, 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. 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 the targeted cytoskeletal proteins and pathways or produce commercially viable drugs that safely and effectively treat cancer, 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 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. In the event that our issued patents and our patent applications, if granted, do not adequately describe, enable or otherwise provide coverage of our technologies and drug candidates, including for example ispinesib, SB-743921, GSK-923295 and CK-1827452, we would not be able to exclude others from developing or commercializing these drug candidates and potential drug candidates. 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 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 without infringing our intellectual property rights;
- some or all of our or our licensors pending patent applications may not result in issued patents;
- our and our licensors issued patents may not provide a basis for commercially viable drugs or therapies, or may not provide us with any competitive advantages, or may be challenged and invalidated by third parties;
- our or our licensors patent applications or patents may be subject to interference, opposition or similar administrative proceedings;
- we may not develop additional proprietary technologies or drug candidates that are patentable; or
- the patents of others may prevent us or our partners from discovering, developing or commercializing our drug candidates.

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. In addition, confidentiality agreements, if any, executed by such persons may not be enforceable or provide meaningful protection for our trade secrets or other

proprietary information in the event of unauthorized use or disclosure. 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 information that is equivalent to our trade secrets, 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 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., or Curis, 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 hedgehog pathway using certain such compounds. Curis has pending applications in Europe, Japan, Australia and Canada with claims covering certain quinazolinone compounds, compositions thereof and/or methods of their use. We are also aware that two of the Australian applications have been allowed and two of the European applications have been granted. In Europe, Australia and elsewhere, the grant of a patent may be opposed by one or more parties. We have opposed the granting of certain such patents to Curis in Europe and in Australia. A third party has also opposed the grant of one of Curis European patents. Curis or a third party may assert that the sale of ispinesib 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 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, Eli Lilly and Company, or Lilly, Bristol-Myers Squibb, or BMS, Array Biopharma Inc., or Array, and ArQule, Inc., or ArQule). 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 our actions 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 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

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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 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 new drugs 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 continue to finance our future cash needs primarily through

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public or private equity offerings, debt financings and 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 delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or future commercialization initiatives.

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.

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 will decrease.

We expect to expand our development, clinical research, sales 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 Chief Executive Officer, Robert I. Blum, our President, Andrew A. Wolff, M.D., F.A.C.C., our Senior Vice President, Clinical Research and Chief Medical Officer, Sharon A. Surrey-Barbari, our Senior Vice President, Finance and Chief Financial Officer, David J. Morgans, Ph.D., our Senior Vice President of Preclinical Research and Development, Jay K. Trautman, Ph.D., our Vice President of Research, and David W. Cragg, our Vice President of Human Resources. 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. 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.

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 and other diseases for which our compounds may be useful treatments. For example, if approved for marketing by the FDA, depending on the approved clinical indication, our cancer drug candidates such as ispinesib and SB-743921 could compete against existing cancer treatments such as paclitaxel, docetaxel, vincristine, vinorelbine or navelbine and potentially against other novel cancer drug candidates that are currently in development such as those that are reformulated taxanes, other tubulin binding compounds or epothilones. We are also aware that Merck, Lilly, Array, BMS, ArQule and others are conducting research and development focused on KSP and other mitotic kinesins. In addition, BMS, Merck, Novartis, Genentech, Inc. and other pharmaceutical and biopharmaceutical companies are developing other approaches to inhibiting mitosis.

With respect to heart failure, if CK-1827452 or any other of our compounds is approved for marketing by the FDA for heart failure, that compound could compete against current generically available therapies, such as milrinone, dobutamine or digoxin or newer drugs such as nesiritide, as well as potentially against other novel drug candidates in development such as ularitide, which is being developed by PDL Biopharma, Inc., urocortin II, which is being developed by Neurocrine Biosciences, Inc., and levosimendan, which is being developed in the United States by Abbott Laboratories and is commercially available in a number of countries outside of the United States.

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;
- hold or obtain proprietary rights that could prevent us from commercializing our products;
- initiate or withstand substantial price competition more successfully than we can;
- more successfully recruit 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;

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

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. 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:

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 efficacious 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