

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 isipinesib 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 isipinesib. We cannot engage a strategic partner for isipinesib 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 isipinesib 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 isipinesib, 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 ispinosib, 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





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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



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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 ispinosib, 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

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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 isspinesib 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,

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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 may prevent our partners or us from obtaining approvals to commercialize 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 Cytokinetics' drug candidates. Obtaining approval of an NDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with the FDA and other applicable foreign and U.S. 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

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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, but not limited to:

a drug candidate may not be safe or effective;

the FDA 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

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 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, or the discovery that adverse effects or toxicities previously observed in preclinical research or clinical trials that were believed to be minor actually constitute much more serious problems, 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 coverage and 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; or

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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.

**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. If we are unable to obtain adequate coverage and reimbursement for our potential drugs, our ability to generate revenue may be adversely affected. 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 and reimbursement 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.**

The use of our drug candidates in clinical trials may result in adverse effects. We currently maintain product liability insurance. We cannot predict all the possible harms or adverse 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, or that third parties that have agreed to indemnify us do not fulfill their obligations. 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, they 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 we or our employees 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

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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 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 is 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 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 Our Common Stock and the Offering**

### **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 volatility in the market price of our common stock include, but are not limited to:

results from, delays in, or discontinuation of, any of the clinical trials for our drug candidates for the treatment of cancer or heart failure, including the current and proposed clinical trials for ispinesib, SB-743921 and GSK-923295 for cancer, and CK-1827452 for heart failure, and



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including delays resulting from slower than expected or suspended patient enrollment or discontinuations resulting from a failure to meet pre-defined clinical end-points;

developments in establishing new strategic alliances;

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

announcements concerning clinical trials;

failure or delays in entering additional drug candidates into clinical trials;

failure or discontinuation of any of our research programs;

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

market conditions in the pharmaceutical, biotechnology and other healthcare related 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 coverage and reimbursement policies;

FDA or other U.S. or foreign regulatory actions affecting us or our industry;

litigation or public concern about the safety of our drug candidates or drugs;

additions or departures of key personnel; or

volatility in the stock prices of other companies in our industry.

These and other external factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert our management's time and attention.

**If the ownership of our common stock continues to be highly concentrated, it may prevent you and other stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause our stock price to decline.**

As of November 30, 2006, our executive officers, directors and their affiliates beneficially owned or controlled approximately 30.2% percent of the outstanding shares of our common stock (after giving effect to the exercise of all outstanding vested and unvested options and warrants). Accordingly, these executive officers, directors and their affiliates, acting as a group, will have substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of us, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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**Evolving regulation of corporate governance and public disclosure may result in additional expenses and continuing uncertainty.**

Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new Securities and Exchange Commission regulations and Nasdaq Global Market, or Nasdaq, rules are creating uncertainty for public companies. We are presently evaluating and monitoring developments with respect to new and proposed rules and cannot predict or estimate the amount of the additional costs we may incur or the timing of such costs. For example, compliance with the internal control requirements of Sarbanes-Oxley Section 404 has to date required the commitment of significant resources to document and test the adequacy of our internal control over financial reporting. While our assessment, testing and evaluation of the design and operating effectiveness of our internal control over financial reporting resulted in our conclusion that as of December 31, 2005 our internal control over financial reporting was effective, we can provide no assurance as to conclusions of management or by our independent registered public accounting firm with respect to the effectiveness of our internal control over financial reporting in the future. These new or changed laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest the resources necessary to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, due to ambiguities related to practice or otherwise, regulatory authorities may initiate legal proceedings against us and our reputation and business may be harmed.

**Volatility in the stock prices of other companies may contribute to volatility in our stock price.**

The stock market in general, and Nasdaq and the market for technology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. Further, there has been particular volatility in the market prices of securities of early stage and development stage life sciences companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs, potential liabilities and the diversion of management's attention and resources.

**We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.**

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our businesses. In addition, the terms of existing or any future debts may preclude us from paying these dividends.

**Our common stock is thinly traded and there may not be an active, liquid trading market for our common stock.**

There is no guarantee that an active trading market for our common stock will be maintained on Nasdaq, or that the volume of trading will be sufficient to allow for timely trades. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active or if trading volume is limited. In addition, if trading



volume in our common stock is limited, trades of

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relatively small numbers of shares may have a disproportionate effect on the market price of our common stock.

**Investors in this offering will pay a much higher price than the book value of our stock.**

If you purchase common stock in this offering, you will incur immediate and substantial dilution of \$ , representing the difference between our net tangible book value as of September 30, 2006 and the as adjusted net tangible book value per share after giving effect to this offering at a price of \$ per share. In the past, we have issued options to acquire common stock at prices significantly below this offering price. To the extent these outstanding options are ultimately exercised, you will incur additional dilution. See Dilution.

**Risks Related To The Committed Equity Financing Facility With Kingsbridge**

**Our committed equity financing facility with Kingsbridge may not be available to us if we elect to make a draw down, may require us to make additional blackout or other payments to Kingsbridge, and may result in dilution to our stockholders.**

In October 2005, we entered into the CEFF with Kingsbridge. The CEFF entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years, shares of our common stock for cash consideration up to an aggregate of \$75.0 million, subject to certain conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless certain conditions are met, which include a minimum price for our common stock; the accuracy of representations and warranties made to Kingsbridge; compliance with laws; effectiveness of a registration statement registering for resale the shares of common stock to be issued in connection with the CEFF and the continued listing of our stock on Nasdaq. In addition, Kingsbridge is permitted to terminate the CEFF if it determines that a material and adverse event has occurred affecting our business, operations, properties or financial condition and if such condition continues for a period of 10 days from the date Kingsbridge provides us notice of such material and adverse event. If we are unable to access funds through the CEFF, or if the CEFF is terminated by Kingsbridge, we may be unable to access capital on favorable terms or at all.

We are entitled, in certain circumstances, to deliver a blackout notice to Kingsbridge to suspend the use of the resale registration statement and prohibit Kingsbridge from selling shares under the resale registration statement. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the resale registration statement is not effective in circumstances not permitted by the agreement, then we must make a payment to Kingsbridge, or issue Kingsbridge additional shares in lieu of this payment, calculated on the basis of the number of shares held by Kingsbridge (exclusive of shares that Kingsbridge may hold pursuant to exercise of the Kingsbridge warrant) and the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the trading price of our common stock declines during a suspension of the resale registration statement, the blackout or other payment could be significant.

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effective on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to 10 percent from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

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**DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS**

In addition to the other information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, you should carefully consider the risk factors disclosed in this prospectus supplement and the accompanying prospectus when evaluating an investment in our securities. This prospectus supplement contains forward-looking statements that are based upon current expectations that are within the meaning of the Private Securities Reform Act of 1995. It is the Company's intent that such statements be protected by the safe harbor created thereby.

Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to, statements regarding:

- the initiation and scope clinical trials and development for our drug candidates and potential drug candidates;
- our plans or ability to commercialize drugs, with or without a partner;
- increasing expenditures and losses;
- the sufficiency of existing resources to fund our operations for at least the next 12 months;
- expansion of the scope and size of research and development efforts;
- potential competitors;
- our needs for additional financing;
- expected future sources of revenue and capital;
- protection of our intellectual property;
- issuance of shares of our common stock under the CEFF; and
- increasing the number of our employees and recruiting additional key personnel.

Factors that could cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those more fully described in the Risk Factors section of this prospectus supplement and accompanying prospectus and elsewhere in this prospectus supplement and in the accompanying prospectus. We undertake no obligation to update or revise these forward-looking statements to reflect events or circumstances after the date of this prospectus supplement except as required by law.

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**USE OF PROCEEDS**

Based upon an offering price of \$      per share, we estimate that the net proceeds we will receive from the sale of shares of our common stock in this offering will be approximately \$      , after deducting the placement agents' fee and estimated offering expenses payable by us. We will retain broad discretion over the use of the net proceeds from the sale of our common stock offered hereby. We currently intend to use the net proceeds from the sale of our common stock in this offering primarily for:

- research and development, including clinical trials for our drug candidates; and
- working capital and other general corporate purposes.

The amounts and timing of the expenditures may vary significantly depending on numerous factors, such as the progress of our research and development efforts, technological advances and the competitive environment for our products. We may also use a portion of the net proceeds to acquire or invest in complementary businesses, products and technologies. Although we currently have no material agreements or commitments with respect to acquisitions, we evaluate acquisition opportunities and engage in related discussions from time to time.

Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

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**DESCRIPTION OF COMMON STOCK**

Please read the information discussed under the heading "Description of Capital Stock" beginning on page 21 of the accompanying prospectus dated June 14, 2005. As of September 30, 2006, 37,793,573 shares of common stock were issued and outstanding.

Upon completion of the sale under this prospectus supplement, approximately \_\_\_\_\_ shares of our common stock will be outstanding, based on the approximate number of shares of common stock issued and outstanding as of September 30, 2006.

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Pro forma net tangible book value dilution per share to investors in this offering represents the difference between the amount per share paid by these investors and the net tangible book value per share of our common stock immediately after completion of this offering. After giving effect to the sale of the \_\_\_\_\_ shares of our common stock being offered in this offering, assuming a purchase price of \$ \_\_\_\_\_ per share and after deducting our estimated offering expenses, our net tangible book value as of September 30, 2006 would have been \$ \_\_\_\_\_ per share. This amount represents an immediate increase in net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and an immediate dilution in net tangible book value of \$ \_\_\_\_\_ per share to investors in this offering as illustrated in the following table:

Assumed price per share		\$
Net tangible book value per share as of September 30, 2006	\$	
Increase in net tangible book value per share attributable to this offering	\$	
Pro forma net tangible book value per share as of September 30, 2006 after giving effect to this offering		
Dilution per share to investors in this offering		\$

The number of shares of our common stock in the computations above excludes the following options and warrants outstanding as of September 30, 2006:

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 employee stock purchase plan.

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**PLAN OF DISTRIBUTION**

We are offering the shares of our common stock through placement agents. Subject to the terms and conditions contained in the placement agent agreement dated December , 2006, Lazard Capital Markets LLC, JMP Securities LLC and Rodman & Renshaw, LLC have agreed to act as the placement agents for the sale of up to shares of our common stock. The placement agents are not purchasing or selling any shares by this prospectus supplement, nor are they required to arrange for the purchase or sale of any specific number or dollar amount of shares, but have agreed to use best efforts to arrange for the sale of all shares.

The placement agent agreement provides that the obligations of the placement agents and the investors are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of certain opinions, letters and certificates from our counsel, our independent auditors and us.

Confirmations and definitive prospectuses will be distributed to all investors who agree to purchase the common stock, informing investors of the closing date as to such shares. We currently anticipate that closing of the sale of shares of common stock will take place on or about December , 2006. Investors will also be informed of the date and manner in which they must transmit the purchase price for their shares.

On the scheduled closing date, the following will occur:

we will receive funds in the amount of the aggregate purchase price; and

Lazard Capital Markets LLC will receive the placement agents fee in accordance with the terms of the placement agent agreement.

We will pay the placement agents a commission equal to 5% of the gross proceeds of the sale of shares of common stock in the offering. We may also reimburse the placement agents for certain legal expenses incurred by them. In no event will the total amount of compensation paid to the placement agents and other securities brokers and dealers upon completion of this offering exceed 8% of the gross proceeds of the offering. The estimated offering expenses payable by us, in addition to the placement agents fee of \$ , are approximately \$195,000, which includes legal, accounting and printing costs and various other fees associated with registering and listing the common stock. After deducting certain fees due to the placement agents and our estimated offering expenses, we expect the net proceeds from this offering to be approximately \$ .

Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith.

We have agreed to indemnify the placement agents and Lazard Frères & Co. LLC against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the placement agent agreement. We have also agreed to contribute to payments the placement agents and Lazard Frères & Co. LLC may be required to make in respect of such liabilities.

We, along with our executive officers and directors, have agreed to certain lock-up provisions with regard to future sales of our common stock for a period of ninety (90) days after the offering as set forth in the placement agent agreement. The 90 day lock-up period described in the preceding paragraph will be extended if:

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during the last 17 days of the initial 90-day lock-up period, we issue an earnings release or material news, or a material event relating to us occurs; or

prior to the expiration of the initial 90-day lock-up period, we announce that we will release earnings results during the 16-day period beginning on the last day of the initial 90-day lock-up period,

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then in each case the initial 90-day lock-up period will be extended until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event, unless Lazard Capital Markets LLC, waives, in writing, such extension.

The placement agent agreement will be included as an exhibit to our Current Report on Form 8-K that we will file with the SEC in connection with the consummation of this offering.

The transfer agent for our common stock to be issued in this offering is Mellon Investor Services LLC.

Our common stock is traded on the Nasdaq Global Market under the symbol CYTK.

The price per share of the common stock will be determined based on negotiations with the purchasers and discussions with the placement agents.

**LEGAL MATTERS**

The validity of the common stock offered hereby will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Thelen Reid Brown Raysman & Steiner LLP in New York, New York is acting as counsel for the placement agents in connection with various matters related to the common stock offered hereby.

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**PROSPECTUS**

**\$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.**



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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.

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**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.

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**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 U.S. 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.

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

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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 U.S. 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 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. 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 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





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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 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 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 clinical 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.

### **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

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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 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



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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 clinical trials or will proceed with such clinical 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 U.S. The patent situation outside the U.S. is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the U.S. 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;

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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 U.S. 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 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 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 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





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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 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;

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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 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.

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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.

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 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 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.



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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.

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





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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, 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

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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:

- 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 U.S. 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 U.S. 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;



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

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.

**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,

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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 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





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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 ispiresib and SB-743921, and including delays resulting from slower than expected patient enrollment in such clinical trials;

- 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;

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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 U.S. or foreign regulatory actions affecting us or our industry;

litigation or public concern about the safety of our drug candidates or drugs;

additions or departures of key personnel; and

volatility in the stock prices of other companies in our industry.

These and other external factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock has been. In addition, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

**If the ownership of our common stock continues to be highly concentrated, it may prevent you and other stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause our stock price to decline.**

As of March 30, 2005, our executive officers, directors and their affiliates beneficially owned or controlled approximately 39% percent of the outstanding shares of our common stock (after giving effect to the exercise of all outstanding vested and unvested options and warrants). Accordingly, these executive officers, directors and their affiliates, acting as a group, will have substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of us, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

**Future sales of common stock by our existing stockholders may cause our stock price to fall.**

The market price of our common stock could decline as a result of sales by our existing stockholders of shares of common stock in the market after our initial public offering, or the perception that these sales could occur. These sales might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate. The lock-up agreements delivered by our executive officers and directors, and substantially all of our stockholders and option holders, in connection with our initial public offering on April 29, 2004, expired on October 27, 2004. Subject to applicable securities law restrictions and other agreements between the company and certain of such stockholders,

these shares are now freely tradable.

**Evolving regulation of corporate governance and public disclosure may result in additional expenses and continuing uncertainty.**

Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new Securities and Exchange Commission

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regulations and Nasdaq National Market rules are creating uncertainty for public companies. We are presently evaluating and monitoring developments with respect to new and proposed rules and cannot predict or estimate the amount of the additional costs we may incur or the timing of such costs. For example, compliance with the internal control requirements of Sarbanes-Oxley Section 404 for the year ended December 31, 2005 requires the commitment of significant resources to document and test the adequacy of our internal controls. While we plan to expend significant resources in developing the required documentation and testing procedures required by Section 404, we can provide no assurance as to conclusions of management or by our independent registered accounting firm with respect to the effectiveness of our internal control over financial reporting. These new or changed laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, due to ambiguities related to practice or otherwise, regulatory authorities may initiate legal proceedings against us and we may be harmed.

**Volatility in the stock prices of other companies may contribute to volatility in our stock price.**

The stock market in general, Nasdaq and the market for technology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. Further, there has been particular volatility in the market prices of securities of early stage and development stage life sciences companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs, potential liabilities and the diversion of management's attention and resources.

**We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.**

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our businesses. In addition, the terms of existing or any future debts may preclude us from paying these dividends.

**Our common stock is thinly traded and there may not be an active, liquid trading market for our common stock.**

There is no guarantee that an active trading market for our common stock will be maintained on Nasdaq, or that the volume of trading will be sufficient to allow for timely trades. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active or if trading volume is limited. In addition, if trading volume in our common stock is limited, trades of relatively small numbers of shares may have a disproportionate effect on the market price of our common stock.

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**Risks Relating to the Offered Securities**

**Our stock price may continue to experience fluctuations, which may significantly affect the market price of our common stock and securities convertible into or exchangeable for our common stock.**

The market price of our common stock fluctuates and is expected to continue to be volatile in the future. These price fluctuations may be rapid and severe and may leave investors little time to react. Factors that may affect the market price of our common stock include the risks and uncertainties described above in this prospectus or described in any applicable prospectus supplement, as well as changes in securities analysts' earnings projections or recommendations. These factors could lead to a significant decrease in the market price of our common stock and securities convertible into or exchangeable for our common stock.

**The securities we are offering may not develop an active public market, which could depress the resale price of the securities.**

The securities that we may offer, other than our common stock, will be new issues of securities for which there is currently no trading market. We cannot predict whether an active trading market for the securities will develop or be sustained. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. If an active trading market were to develop, the securities could trade at prices that may be lower than the initial offering price of the securities. We cannot guarantee the liquidity of the trading markets for any securities.

**We will have broad discretion over the use of the proceeds to us from this offering and may apply it to uses that do not improve our operating results or the value of your securities.**

We will have broad discretion to use the net proceeds to us from this offering, and investors will be relying solely on the judgment of our board of directors and management regarding the application of these proceeds. Although we expect to use the net proceeds from this offering for general corporate purposes, we have not allocated these net proceeds for specific purposes. Investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately. Our use of the proceeds may not improve our operating results or increase the value of the securities being offered hereby.

**DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS**

In addition to the other information contained or incorporated by reference in this prospectus, you should carefully consider the risk factors disclosed in this prospectus or any prospectus supplement when evaluating an investment in our securities. This prospectus contains forward-looking statements that are based upon current expectations that are within the meaning of the Private Securities Reform Act of 1995. It is the Company's intent that such statements be protected by the safe harbor created thereby.

Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to, statements regarding:

the potential benefits of our drug candidates and potential drug candidates;

the utility of our proprietary technologies and biological focus;

our plans or ability to commercialize drugs, with or without a partner;

increasing expenditures and losses;

expansion of the scope and size of research and development efforts;



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potential competitors;

our needs for additional financing;

expected future sources of revenue and capital;

protection of our intellectual property; and

increasing the number of our employees and recruiting additional key personnel.

**USE OF PROCEEDS**

Unless otherwise indicated in a prospectus supplement, the net proceeds from the sale of securities offered by this prospectus will be used for general corporate purposes and working capital requirements. We may also use a portion of the net proceeds to fund possible investments in and acquisitions of complementary businesses, partnerships, minority investments, products or technologies. Currently, there are no commitments or agreements regarding such acquisitions or investments that are material. Pending their ultimate use, we intend to invest the net proceeds in money market funds, commercial paper and governmental and non-governmental debt securities.

**RATIO OF EARNINGS AVAILABLE TO COVER FIXED CHARGES**

The ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends for each of the periods indicated is as follows:

	<b>Fiscal Year Ended December 31,</b>					<b>Quarter Ended</b>
	<b>2000</b>	<b>2001</b>	<b>2002</b>	<b>2003</b>	<b>2004</b>	<b>March 31, 2005</b>
Ratio of earnings available to cover fixed charges(1)						
Ratio of earnings available to combined fixed charges and preferred dividends(1)						

(1) Due to our losses in years ended December 31, 2000, 2001, 2002, 2003 and 2004 and the quarter ended March 31, 2005, the ratio coverage was less than 1:1. Additional earnings of \$13.1 million, \$15.9 million, \$23.1 million, \$32.7 million, \$37.2 million and \$10.5 million would have been required in each of those periods, respectively, to achieve a coverage of 1:1

In calculating the ratio of earnings available to cover fixed charges and the ratio of earnings available to cover combined fixed charges and preferred dividends, earnings consists of net income (loss) before provisions for income taxes plus fixed charges. Fixed charges consist of:

interest expense;

amortization of prepayment penalty on debt; and

one-third of our rental expense, which we believe to be representative of interest attributable to rentals.

For the periods set forth in the table above, we had preferred stock outstanding only during 2000, 2001, 2002, 2003 and until April 29, 2004. All outstanding shares of preferred stock were converted into shares of common stock in connection with our initial public offering under our Registration Statement (SEC File No. 333-112261) declared effective by the SEC on April 29, 2004. We have no preferred stock outstanding as of the date of this prospectus.

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**DESCRIPTION OF CAPITAL STOCK**

As of the date of this prospectus, our authorized capital stock consists of 130,000,000 shares. Those shares consist of 120,000,000 shares designated as common stock, \$0.001 par value, and 10,000,000 shares designated as preferred stock, \$0.001 par value. The only equity securities currently outstanding are shares of common stock. As of May 31, 2005, there were approximately 28,615,114 shares of common stock issued and outstanding.

The following description summarizes the material terms of our capital stock. This summary is, however, subject to the provisions of our restated certificate of incorporation and any applicable certificate of designations for a series of preferred stock, and by the provisions of applicable law.

**Common Stock**

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Upon any liquidation, dissolution or winding up of our business, the holders of common stock are entitled to share equally in all assets available for distribution after payment of all liabilities and provision for liquidation preference of shares of preferred stock then outstanding. Holders of common stock have no preemptive rights or rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. Holders of common stock are entitled to receive dividends declared by the board of directors, out of funds legally available for the payment of dividends, subject to the rights of holders of preferred stock. Currently, we are not paying dividends.

Our common stock is listed on The Nasdaq National Market under the symbol CYTK. The transfer agent and registrar for our common stock is Mellon Investor Services LLC. Mellon's address is 235 Montgomery Street, San Francisco, California 94104 and its telephone number is (415) 743-1422.

All outstanding shares of common stock are fully paid and non-assessable, and all shares of common stock offered by this prospectus, or issuable upon conversion or exercise of securities, will, when issued, be validly issued and fully paid and non-assessable.

**Preferred Stock**

Pursuant to our restated certificate of incorporation, our board of directors has the authority, without further approval by the stockholders, to designate and issue up to 10,000,000 shares of preferred stock in one or more series. Cytokinetics board of directors may designate the powers, preferences, privileges and relative participating, optional or special rights and the qualifications, limitations or restrictions of each series of preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights of the common stock. Thus, without stockholder approval, our board of directors could authorize the issuance of preferred stock with voting, conversion and other rights that could dilute the voting power and other rights of holders of our common stock, and may have the effect of decreasing the market price of the common stock.

The description of certain provisions of the preferred stock set forth in any prospectus supplement does not purport to be complete and is subject to and qualified in its entirety by reference to our certificate of incorporation and the certificate of designations relating to each series of preferred stock. The applicable prospectus supplement will describe the specific terms of any series of preferred stock being offered which may include:

the specific designation, number of shares, seniority and purchase price;

any liquidation preference per share and any accumulated dividends upon the liquidation, dissolution or winding up of Cytokinetics affairs;

any date of maturity;

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any redemption, repayment or sinking fund provisions;

any dividend rate or rates, whether dividend rate is fixed or variable, the date dividends accrue, the dates on which any such dividends will be payable (or the method by which such rates or dates will be determined), and whether dividends will be cumulative;

any voting rights;

if other than the currency of the U.S., the currency or currencies (including composite currencies) in which such preferred stock is denominated and in which payments will or may be payable;

the method by which amounts in respect of such series of preferred stock may be calculated and any commodities, currencies or indices, or value, rate or price, relevant to such calculation;

whether such series of preferred stock is convertible and, if so, the securities or rights into which it is convertible, and the terms and conditions upon which such conversions will be effected;

the place or places where dividends and other payments on such series of preferred stock will be payable; and

any additional voting, dividend, liquidation, redemption and other rights, preferences, privileges, limitations and restrictions.

All shares of preferred stock offered by this prospectus, or issuable upon conversion or exercise of securities, will, when issued, be validly issued and fully paid and non-assessable.

**Anti-Takeover Effects of Some Provisions of Delaware Law**

Provisions of Delaware law and our amended and restated certificate of incorporation and amended bylaws could make the acquisition of our company through a tender offer, a proxy contest or other means more difficult and could make the removal of incumbent officers and directors more difficult. We expect these provisions to discourage coercive takeover practices and inadequate takeover bids and to encourage persons seeking to acquire control of our company to first negotiate with our board of directors. We believe that the benefits provided by our ability to negotiate with the proponent of an unfriendly or unsolicited proposal outweigh the disadvantages of discouraging these proposals. We believe the negotiation of an unfriendly or unsolicited proposal could result in an improvement of its terms.

We are subject to Section 203 of the Delaware General Corporation Law, an anti-takeover law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder, unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers, and (b) shares owned by employee stock plans in which employee participants do not have the right to determine;

confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

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on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting securities. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

### **Anti-Takeover Effects of Provisions of Our Charter Documents**

Our amended and restated certificate of incorporation provides for our board of directors to be divided into three classes serving staggered terms. Approximately one-third of the board of directors will be elected each year. The provision for a classified board could prevent a party who acquires control of a majority of the outstanding voting stock from obtaining control of the board of directors until the second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. The classified board provision could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company and could increase the likelihood that incumbent directors will retain their positions. Our amended and restated certificate of incorporation provides that directors may be removed with cause by the affirmative vote of the holders of the outstanding shares of common stock.

Our amended bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. At an annual meeting, stockholders may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors. Stockholders may also consider a proposal or nomination by a person who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given to our Secretary timely written notice, in proper form, of his or her intention to bring that business before the meeting. The amended bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting of the stockholders. However, our bylaws may have the effect of precluding the conduct of business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Under Delaware law, a special meeting of stockholders may be called by the board of directors or by any other person authorized to do so in the amended and restated certificate of incorporation or the amended bylaws. Our amended bylaws authorize a majority of our board of directors, the chairman of the board or the chief executive officer to call a special meeting of stockholders.

Because our stockholders do not have the right to call a special meeting, a stockholder could not force stockholder consideration of a proposal over the opposition of the board of directors by calling a special meeting of stockholders prior to such time as a majority of the board of directors believed or the chief executive officer believed the matter should be considered or until the next annual meeting provided that the requestor met the notice requirements. The restriction on the ability of stockholders to call a special meeting means that a proposal to replace the board also could be delayed until the next annual meeting.





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Delaware law provides that stockholders may execute an action by written consent in lieu of a stockholder meeting. However, Delaware law also allows us to eliminate stockholder actions by written consent. Elimination of written consents of stockholders may lengthen the amount of time required to take stockholder actions since actions by written consent are not subject to the minimum notice requirement of a stockholder's meeting. However, we believe that the elimination of stockholders' written consents may deter hostile takeover attempts. Without the availability of stockholders' actions by written consent, a holder controlling a majority of our capital stock would not be able to amend our bylaws or remove directors without holding a stockholders' meeting. The holder would have to obtain the consent of a majority of the board of directors, the chairman of the board or the chief executive officer to call a stockholders' meeting and satisfy the notice periods determined by the board of directors. Our amended and restated certificate of incorporation provides for the elimination of actions by written consent of stockholders upon the closing of this offering.

**DESCRIPTION OF THE WARRANTS**

**General**

We may issue warrants for the purchase of our common stock or preferred stock or any combination thereof. Warrants may be issued independently or together with our common stock or preferred stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;
- the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;
- the dates on which the right to exercise the warrants shall commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

the currency or currency units in which the offering price, if any, and the exercise price are payable;  
if applicable, a discussion of material U.S. federal income tax considerations;

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the antidilution provisions of the warrants, if any;

the redemption or call provisions, if any, applicable to the warrants;

any provisions with respect to a holder's right to require us to repurchase the warrants upon a change in control; and

any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of warrants will not be entitled:

to vote, consent or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders of Cytokinetics.

As set forth in the applicable prospectus supplement, the exercise price and the number of shares of common stock purchasable upon exercise of the warrant will be subject to adjustment in certain events, including the issuance of a stock dividend to any holders of common stock or preferred stock, a stock split, reverse stock split, combination, subdivision or reclassification of common stock or preferred stock, and such other events, if any, specified in the applicable prospectus supplement.

**PLAN OF DISTRIBUTION**

We may sell the securities covered by this prospectus in any of the following ways:

through one or more underwriters or dealers;

through agents;

directly to one or more purchasers; or

through a combination of the above.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Each prospectus supplement will identify any underwriter, dealer or agent, and describe any compensation received by them from us. Any initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers as their agents in connection with the sale of the securities. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by underwriters, dealers or agents may be treated as underwriting discounts and commissions.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may grant underwriters who participate in the distribution of the securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution. We will identify the amount of any such over-allotment option in the applicable prospectus supplement.

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We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent and the terms of any agency relationship in the prospectus supplement. We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may distribute the securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to prevailing market prices; and

at negotiated prices.

A prospectus supplement or supplements will describe the method of distribution of each distribution of securities in the applicable prospectus supplement.

We may determine the price or other terms of the securities offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the underwriters' obligations in the related supplement to this prospectus.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

In connection with the offering of the securities, certain persons participating in such offering may engage in transactions that stabilize, maintain or otherwise affect the market price, including over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the common stock in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer is purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. The securities may or may not be listed on a national securities exchange or traded in the over-the-counter market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions in the securities on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest

independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

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To the extent required, this prospectus may be amended and supplemented from time to time to describe a specific plan of distribution.

**LEGAL MATTERS**

The validity of securities offered hereby will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California.

**EXPERTS**

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2004 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

**WHERE YOU CAN FIND MORE INFORMATION**

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the shares of common stock we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information, at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC's web site at <http://www.sec.gov>.

**INFORMATION INCORPORATED BY REFERENCE**

The SEC allows us to incorporate by reference into this prospectus the information we filed with the SEC. This means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus. Information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than reports or portions furnished under Items 2.02, 7.01 or 8.01 of Form 8-K) until we complete our offering of the securities offered by this prospectus:

our annual report on Form 10-K for the fiscal year ended December 31, 2004;

our definitive proxy statement on Schedule 14A, filed on April 6, 2005;

our quarterly report on Form 10-Q for the fiscal quarter ended March 31, 2005;

our current reports on Form 8-K dated January 6, 2005, February 7, 2005, March 28, 2005, March 30, 2005, and April 5, 2005; and

the description of our common stock contained in our Registration Statement on Form 8-A, filed with the Securities and Exchange Commission on March 12, 2004, and any further amendment or report filed hereafter

for the purpose of updating any such description.



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Copies of documents incorporated by reference, excluding exhibits except to the extent such exhibits are specifically incorporated by reference, are available from us without charge, upon oral or written request to:

Cytokinetics, Incorporated  
280 East Grand Avenue  
South San Francisco, California 94080  
United States of America  
Attn: Investor Relations  
(650) 624-3000

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**Shares of Common Stock**

**PROSPECTUS SUPPLEMENT**

**Lazard Capital Markets**

**JMP Securities**

**Rodman & Renshaw**

December , 2006