

CYTOKINETICS INC  
Form 10-K  
March 12, 2008

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

**Form 10-K**

**ANNUAL REPORT UNDER SECTION 13 or 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934**

**(Mark One)**

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2007**
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934**

**Commission file number: 000-50633  
CYTOKINETICS, INCORPORATED**  
*(Exact name of registrant as specified in its charter)*

**Delaware**  
*(State or other jurisdiction of  
incorporation or organization)*

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

**Robert I. Blum  
President and Chief Executive Officer  
280 East Grand Avenue  
South San Francisco, CA 94080  
(650) 624-3000**

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

**Securities registered pursuant to Section 12(b) of the Act:  
Common Stock, \$0.001 par value**

**Securities registered pursuant to Section 12(g) of the Act:  
None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

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Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes  No

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

|   |   |   |  |
|---|---|---|--|
| Large accelerated filer <input type="radio"/> | Accelerated<br>filer <input checked="" type="radio"/> | Non-accelerated filer <input type="radio"/><br>(Do not check if a smaller reporting<br>company) | Smaller reporting<br>company <input type="radio"/> |
|---|---|---|--|

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the voting and non-voting common equity held by non-affiliates was \$184.0 million computed by reference to the last sales price of \$5.65 as reported by the NASDAQ Global Market, as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2007. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose.

The number of shares outstanding of the Registrant's common stock on February 29, 2008 was 49,301,300 shares.

### DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2008 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission, are incorporated by reference to Part III of this Annual Report on Form 10-K.

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**CYTOKINETICS, INCORPORATED**

**FORM 10-K  
Year Ended December 31, 2007**

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**PART I**

This report contains forward-looking statements that are based upon current expectations within the meaning of the Private Securities Litigation Reform Act of 1995. We intend 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 about or relating to:

the initiation, progress, timing and scope of clinical trials and development for our drug candidates and potential drug candidates by ourselves, GlaxoSmithKline, or GSK, or the National Cancer Institute, or NCI, including the anticipated timing for initiation of clinical trials, and anticipated dates of data becoming available or being announced from clinical trials;

guidance concerning revenues, research and development expenses and general and administrative expenses for 2008;

the identification and advancement of additional potential drug candidates into preclinical studies and clinical trials;

our and our partners' plans or ability for continued research and development of drug candidates, such as CK-1827452, ispinesib, SB-743921 and GSK-923295;

our ability to generate clinical data sufficient to result in Amgen Inc., or Amgen, exercising its option with respect to CK-1827452 or GSK exercising its option with respect to either or both of ispinesib or SB-743921, or to provide such data within our expected timeframes;

our expected roles in research, development or commercialization under our strategic alliances, such as with Amgen and GSK;

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

the scope and size of our research and development activities and programs;

the utility of the clinical trials programs for our drug candidates to inform future development activities;

our plans or ability to commercialize drugs with or without a partner, including our intention to develop sales and marketing capabilities;

receipt of milestone payments, royalties and other funds from our partners under strategic alliances, such as with Amgen, and GSK;

issuance of shares of our common stock under our committed equity financing facility, or CEFF, entered into with Kingsbridge Capital Limited, or Kingsbridge, in 2007;

losses, costs, expenses and expenditures;

the sufficiency of existing resources to fund our operations for at least the next 12 months;

capital requirements and our needs for additional financing;  
future payments under lease obligations and equipment financing lines;  
expected future sources of revenue and capital;  
our ability to protect our intellectual property and avoid infringing the intellectual property rights of others;  
potential competitors and competitive products;  
our plans to obtain limited product liability insurance;  
increasing the number of our employees and recruiting additional key personnel; and  
expected future amortization of employee stock-based compensation.

Such forward-looking statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to:

difficulties or delays in development, testing, obtaining regulatory approval for, and undertaking production and marketing of our drug candidates, including decisions by the NCI to postpone or discontinue research or

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development activities for ispinesib, or by GSK to postpone or discontinue research or development activities relating to centromere-associated protein E, or CENP-E, or GSK-923295;

difficulties or delays in or slower than anticipated patient enrollment in our or our partners' clinical trials;

unexpected adverse side effects or inadequate therapeutic efficacy of our drug candidates that could slow or prevent product approval (including the risk that current and past results of clinical trials or preclinical studies are not indicative of future results of clinical trials);

the possibility that the U.S. Food and Drug Administration, or FDA, or foreign regulatory agencies may delay or limit our or our partners' ability to conduct clinical trials;

the receipt of funds by us under our strategic alliances, including those funds dependent upon Amgen's exercise of its option with respect to CK-1827452 and GSK's exercise of its option with respect to either or both of ispinesib and SB-743921;

activities and decisions of, and market conditions affecting, current and future strategic partners;

our ability to obtain additional financing if necessary;

our ability to maintain the effectiveness of current public information under our registration statement permitting resale of securities to be issued to Kingsbridge by us under, and in connection with, the 2007 CEFF;

changing standards of care and the introduction of products by competitors or alternative therapies for the treatment of indications we target;

the uncertainty of protection for our intellectual property, through patents, trade secrets or otherwise; and

potential infringement of the intellectual property rights or trade secrets of third parties.

In addition such statements are subject to the risks and uncertainties discussed in the "Risk Factors" section and elsewhere in this document. Operating results are not necessarily indicative of results that may occur in future periods.

When used in this report, unless otherwise indicated, "Cytokinetics," "the Company," "we," "our" and "us" refers to Cytokinetics, Incorporated.

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

**Item 1. Business**

**Overview**

We are a biopharmaceutical company, incorporated in Delaware in 1997, focused on developing small molecule therapeutics for the treatment of cardiovascular diseases and cancer. Our current development activities are primarily directed to advancing multiple drug candidates through clinical trials with the objective of determining the intended pharmacodynamic effect or effects in two principal diseases: heart failure and cancer. Our drug development pipeline consists of a drug candidate, CK-1827452, being developed in both an intravenous and oral formulation for the



potential treatment of heart failure, and three drug candidates, ispinesib, SB-743921 and GSK-923295, each being developed in an intravenous formulation for the potential treatment of cancer. Our drug candidates are all novel small molecules that arose from our research activities and are directed toward the biology of the cytoskeleton. We believe our understanding of the cytoskeleton enables us to discover novel and potentially safer and more effective therapeutics.

CK-1827452, our drug candidate for the treatment of heart failure, is an activator of cardiac myosin, a cytoskeletal protein in the heart muscle. We initiated Phase I clinical trials with CK-1827452, administered both intravenously and orally, in 2006. In 2007, we initiated a clinical trials program for CK-1827452, comprised of Phase I and Phase IIa trials, designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of both an intravenous and oral formulations of CK-1827452 in a diversity of patients, including patients with stable heart failure and patients with ischemic cardiomyopathy. The first Phase IIa clinical trial from this program, initiated in April 2007, is a multi-center, double-blind, randomized, placebo-controlled, dose-escalation

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study designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of an intravenous formulation of CK-1827452 in patients with stable heart failure. We also initiated three Phase I clinical trials from this program in 2007: one to evaluate potential drug-drug interactions with CK-1827452, one to evaluate the pharmacokinetics of an oral formulation of CK-1827452 given in multiple doses and one to assess the pharmacokinetics and relative bioavailability of three different oral modified release prototypes of CK-1827452. We plan to initiate two additional Phase IIa clinical trials within this program in 2008. Our goal is to develop CK-1827452 as a potential treatment across the continuum of care in heart failure, both in the hospital setting as an intravenous formulation for acutely decompensated heart failure and in the outpatient setting as an oral formulation for chronic heart failure. CK-1827452 is being developed in connection with a strategic alliance that we established with Amgen in December 2006, pursuant to which Amgen obtained an option to participate in the future development and commercialization of CK-1827452. This option is exercisable during a defined period, the ending of which is dependent upon the satisfaction of certain conditions, primarily the delivery of Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed development plan, the results from which may be sufficient to support its progression into Phase IIb clinical development.

Our oncology development program includes our drug candidates ispinesib, SB-743921 and GSK-923295. We are currently conducting Phase I/II clinical trials of ispinesib and SB-743921. GSK-923295 is being developed in connection with our strategic alliance with GSK established in 2001. This strategic alliance is focused on novel small molecule therapeutics targeting a family of cytoskeletal proteins known as mitotic kinesins for the treatment of cancer. Ispinesib, our most advanced anti-cancer drug candidate, is an inhibitor of kinesin spindle protein, or KSP. Ispinesib has been the subject of a broad Phase II clinical trials program under the sponsorship of GSK and the NCI designed to evaluate the effectiveness of this drug candidate in multiple tumor types. We have reported Phase II clinical trials data from this program in metastatic breast, non-small cell lung, ovarian, colorectal, head and neck, hepatocellular, renal and prostate cancers and melanoma. To date, we believe clinical activity for ispinesib has been observed in non-small cell lung, ovarian and breast cancers, with the most robust clinical activity observed in a Phase II clinical trial evaluating ispinesib in the treatment of patients with locally advanced or metastatic breast cancer that had failed treatment with taxanes and anthracyclines. We are conducting, at our expense, a focused development program for ispinesib in breast cancer that is specifically designed to supplement the Phase I and Phase II clinical trials sponsored by GSK that demonstrated clinical activity in the treatment of patients with metastatic breast cancer and also demonstrated an acceptable tolerability profile for ispinesib in combination with capecitabine. As part of this development program, in December 2007, we initiated an open-label, non-randomized Phase I/II clinical trial that is designed to evaluate ispinesib as monotherapy, as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer.

SB-743921 is our second drug candidate that inhibits KSP and is currently being studied, at our expense, in a Phase I/II clinical trial evaluating its safety and tolerability in patients with Hodgkin or non-Hodgkin lymphoma. In December 2007, at the Annual Meeting of the American Society of Hematology, a poster was presented summarizing interim data from Phase I of this clinical trial. We anticipate final data from the Phase I portion of this trial to be available in the first half of 2008. We are currently responsible for the conduct, at our expense, of any further development of ispinesib and SB-743921. GSK retains an option to resume the development and commercialization of either or both of ispinesib and SB-743921, exercisable during a defined period.

GSK-923295 is the third drug candidate to emerge from our strategic alliance with GSK and is an inhibitor of a different mitotic kinesin, CENP-E. In August 2007, we announced that GSK initiated a first-time-in-humans Phase I clinical trial of GSK-923295. This trial is an open-label, non-randomized, dose-finding trial designed to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of GSK-923295 in patients with solid tumors. Cytokinetics and GSK are also conducting collaborative research activities directed to inhibitors of CENP-E, including GSK-923295.

In both heart failure and cancer, we intend to conduct clinical trials of our drug candidates throughout 2008 with the objective of determining the intended pharmacodynamic effect or effects to inform potential advancement of these drug candidates into late-stage registration clinical trials.

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The following chart shows the status of our current on-going and planned clinical trials as of February 29, 2008. Each clinical trial indicated in the chart should be viewed in conjunction with its respective Status :

\* Status based on Phase II clinical trials program conducted by GSK and the NCI.

- (1) Sponsored by the NCI
- (2) Sponsored by Cytokinetics
- (3) Sponsored by GSK

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In addition to the above clinical programs, we have other research programs that we believe may contribute to our development pipeline over time. All of our drug candidates and potential drug candidates were discovered by leveraging our drug discovery expertise focused on the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. We believe the cytoskeleton is one of a few biological areas with broad potential for drug discovery and development and has been scientifically and commercially validated in a wide variety of human diseases. For example, the cardiac sarcomere, a cytoskeletal structure in the cardiac muscle cell, plays a fundamental role in cardiac contraction. Heart failure is a syndrome often caused by impaired cardiac contractility. We have discovered and are developing small molecules that are designed to activate the cardiac sarcomere and to cause an increase in cardiac contractility as a potential new way to treat heart failure. The cytoskeleton also plays a fundamental role in cell proliferation, and cancer is a disease of unregulated cell proliferation. Hence, small molecule inhibitors of these cytoskeletal proteins may prevent cancer cells from proliferating. We believe that our knowledge of the cytoskeleton has enabled us to discover novel and potentially safer and more effective classes of drugs directed at the treatment of cardiovascular diseases, cancer and other diseases. We are also conducting research with respect to compounds that may modulate other cellular targets, including cytoskeletal targets, that may have utility in other disease areas. We have developed a cell biology driven approach and proprietary technologies, such as our PUMA™ system and our Cytometrix® technologies, to evaluate the function of many interacting proteins in the complex environment of the intact human cell. We believe that this enables us to efficiently focus our activities towards those compounds directed at novel protein targets that we feel are more likely to yield attractive drug candidates.

We selectively seek partners and strategic alliances that enable us to maintain financial and operational flexibility while retaining significant economic and commercial rights to our drug candidates. For example, in December 2006, we entered into a collaboration and option agreement with Amgen under which we are conducting research with activators of cardiac myosin in order to identify potential treatments for patients with heart failure. Pursuant to that agreement, we granted Amgen an option for the joint development and commercialization of CK-1827452, world-wide except Japan. The option is exercisable during a defined period, the ending of which is dependent upon the satisfaction of certain conditions, primarily the delivery of Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed development plan, the results from which may be sufficient to support its progression into Phase IIb clinical development. Under this strategic alliance, we retain the right to elect to co-fund later-stage development of CK-1827452, which would provide us with an opportunity to earn enhanced royalties on the sales of resulting drugs, if any, and the right to co-promote such drugs. In 2001, we entered into a collaboration and license agreement with GSK, or the GSK Agreement, to conduct research and development activities focused towards the potential treatment of cancer through the inhibition of mitotic kinesins. Our drug candidates ispinesib, SB-743921 and GSK-923295 arose from that strategic alliance. Ispinesib has been the subject of a broad clinical trials program conducted by both GSK and the NCI under the strategic alliance. Pursuant to a November 2006 amendment to the GSK Agreement, we assumed responsibility for the costs and activities of the continued development of ispinesib and SB-743921 and granted GSK an option to resume the development and commercialization of ispinesib and SB-743921, exercisable during a defined period. Cytokinetics and GSK continue to conduct collaborative research activities directed to CENP-E and GSK continues to develop GSK-923295. We retain the right to elect to co-fund later-stage development of these drug candidates, which would provide us with an opportunity to earn enhanced royalties on the sales of resulting drugs, if any, and the right to co-promote such drugs. In the future, we may seek to form strategic alliances relating to compounds arising from our research programs directed to skeletal and smooth muscle contractility.

We may develop commercial capabilities to address markets characterized by severe illnesses, large patient populations and concentrated customer groups. For example, should CK-1827452 or any compounds from our cardiovascular program be approved for the treatment of heart failure, we intend to develop the sales and marketing capabilities necessary to support their commercialization in North America. Similarly, should any of ispinesib, SB-743921 or GSK-923295 be approved for the treatment of cancer, we intend to establish sales and marketing

capabilities to support the commercialization of one or more of them in North America. In markets for which customer groups are not concentrated, we intend to seek strategic alliances for the development of our drug candidates and potential drug candidates and the commercialization of the resulting drugs, if any, while retaining significant financial interests.

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**Our Corporate Strategy**

Our goal is to become a fully-integrated biopharmaceutical company focused on discovering, developing and commercializing novel drugs to treat cardiovascular diseases, cancer and other diseases. We intend to achieve this goal by:

***Continuing to focus our drug discovery and development activities on two core areas: cardiovascular diseases and oncology.***

We have focused our drug discovery and development activities on cardiovascular diseases and oncology as these represent large commercial markets with unmet medical needs. Our focus on the cytoskeleton has yielded first-generation drug candidates in these therapeutic areas and has validated the cytoskeleton as a target for our drug discovery activities. Our drug discovery and development programs are directed to potential next-generation pharmaceuticals that may offer additional treatment opportunities in these therapeutic areas and also address potential liabilities of existing first-generation approaches.

***Conducting multiple clinical trials across each of several related disease indications and associated patient populations***

For select drug candidates, we intend to conduct multiple clinical trials across each of several related disease indications and associated patient populations, working internationally as necessary to gain access to appropriate cohorts of patients. We believe that by pursuing this approach we increase the probability these drug candidates may achieve positive outcomes in clinical trials and thereby may also increase the commercial potential of these drug candidates.

***Establishing select strategic alliances to support our drug development programs while preserving significant development and commercial rights.***

We intend to enter selectively into strategic alliances to support our drug discovery and development programs or technologies, to obtain financial support and to leverage the therapeutic area expertise and development and commercialization resources of our partners to potentially accelerate the development and commercialization of our drug candidates. As appropriate, we plan to maintain certain rights in joint development of drug candidates and commercialization of potential drugs arising from our alliances so we can build our internal clinical development and sales and marketing capabilities while also maintaining a significant share of the potential revenues for any products arising from each alliance.

***Building development and commercialization capabilities directed at large concentrated markets.***

We focus our drug discovery and development activities on large commercial market opportunities in concentrated customer segments, such as heart failure and cancer. By focusing on concentrated markets, we believe that a company at our stage of development can compete effectively within these markets against larger, more established companies with greater financial resources. For each opportunity focused on these markets, we intend to develop clinical development and sales and marketing capabilities in order to become a fully-integrated biopharmaceutical company that can develop and commercialize drugs that arise from our research and development programs.

***Leveraging our cytoskeletal expertise, cell biology-driven approach and proprietary technologies to increase the speed, efficiency and yield of our drug discovery and development processes.***

We have focused our drug discovery activities on the cytoskeleton because its role in disease has been scientifically and commercially validated. We believe that our unique understanding of the cytoskeleton will enable us to discover and potentially develop drug candidates with novel mechanisms of action and which may avoid or reduce certain limitations of current drugs. We believe that there are few, if any, other companies that have focused specifically on the cytoskeleton. We intend to pursue drug discovery programs across a number of therapeutic areas and we believe we can leverage research and development investments made for a program directed at one therapeutic area to programs directed at other therapeutic areas. This may facilitate our building a diverse pipeline of drug candidates in a cost-effective fashion.



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We believe that our innovative cell biology-driven research approach and proprietary technologies enhance the speed, efficiency and yield of drug discovery and, potentially, of drug development. We believe we can identify and focus on the most promising compounds earlier in drug discovery by quickly and efficiently eliminating those compounds that lack the desired efficacy or exhibit potential toxicities. As a result, we may save time and resources and reduce the occurrence of later-stage failures, which may result in a higher yield of drug candidates with a greater chance of clinical success.

### ***Pursuing multiple drug candidates for each cytoskeletal protein target.***

For each of our programs, we characterize several drug candidates for each of a number of cytoskeletal protein targets that act together in a protein pathway or in a multi-protein system. By leveraging our drug discovery efficiencies, we intend to identify, for each cytoskeletal protein target, multiple potential drug candidates that we may progress into clinical development. We believe that this approach of pursuing a portfolio of potential drug candidates for each cytoskeletal protein target in parallel allows us to increase our potential for commercial success.

### **Cardiovascular Disease Program**

Our cardiovascular disease program is focused towards the discovery and development of small molecule cardiac myosin activators in order to create next-generation drug candidates to potentially treat acute and chronic heart failure. This program is based on the hypothesis that activators of cardiac myosin may improve heart function by increasing cardiac contractility without triggering the common adverse clinical effects associated with current pharmacological attempts to increase left ventricular systolic function in heart failure patients. Existing drugs that seek to improve cardiac cell contractility typically increase the concentration of intracellular calcium, which indirectly activates cardiac myosin, but also has been linked to potentially life-threatening side effects. In contrast, targeted cardiac myosin activators have been shown to work by a novel mechanism that directly stimulates the activity of the cardiac myosin motor protein without increasing the concentration of intracellular calcium, thereby potentially reducing or avoiding the associated side effects. In animal models, our potential drug candidates from this program improved cardiac contractility without the adverse effects on heart rate and rhythm, blood pressure and oxygen consumption often exhibited by existing drugs that work by increasing intracellular calcium.

CK-1827452 is our first drug candidate to arise from this program, and is being developed in connection with our collaboration with Amgen established in December 2006. In September 2006 and September 2007, we announced data from the first-time-in-humans Phase I clinical trial of CK-1827452 evaluating the safety, tolerability, pharmacodynamics and pharmacokinetic profile of a six-hour intravenous infusion of CK-1827452 in healthy volunteers. In this trial, CK-1827452 was well-tolerated and statistically significant and concentration-dependent increases in indices of left ventricular function were demonstrated. In addition, CK-1827452 exhibited generally linear, dose-proportional pharmacokinetics across the dose range studied. The adverse effects at intolerable doses in humans appeared similar to the adverse findings which occurred at similar plasma concentrations in the preclinical safety studies. These effects are believed to be related to an excess of the intended pharmacologic effect, resulting in excessive prolongation of the systolic ejection time, and resolved promptly with discontinuation of the infusions of CK-1827452. The Phase I clinical trial activity of CK-1827452 is consistent with results from preclinical evaluations of CK-1827452 in normal dogs; however, further clinical trials are necessary to determine whether similar results will also be seen in patients with heart failure.

In December 2006 and September 2007, we announced results from a Phase I study designed to investigate the absolute bioavailability of two oral formulations (liquid and immediate-release solid) of CK-1827452 versus an intravenous dose in healthy volunteers. Pharmacokinetic data from this study demonstrated oral bioavailability of approximately 100% for each of the three conditions of oral administration (i.e., liquid fasted, solid fasted and solid fed). We believe these data support our current activities to develop a modified release oral formulation of

CK-1827452 to enable late-stage clinical development with a dosing schedule that may be suitable for the treatment of patients with chronic heart failure.

In April 2007, we initiated a clinical trials program for CK-1827452 comprised of additional Phase I and Phase IIa trials designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of both the intravenous and oral formulations of CK-1827452 in a diversity of patients, including patients with stable heart failure and patients with ischemic cardiomyopathy. The first clinical trial in this program is a Phase IIa multi-center, double-blind, randomized, placebo-controlled, dose-escalation study designed to evaluate the safety, tolerability,

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pharmacodynamics and pharmacokinetic profile of an intravenous formulation of CK-1827452 in patients with stable heart failure. We also initiated three Phase I clinical trials from this program in 2007, all with oral formulations of CK-1827452: one to evaluate potential drug-drug interactions, one to evaluate the pharmacokinetics of multiple doses and one to assess the pharmacokinetics and relative bioavailability of three different oral modified release prototypes. We plan to initiate two additional Phase IIa clinical trials within this program in 2008. Our goal is to develop CK-1827452 as a potential treatment across the continuum of care in heart failure, both in the hospital setting as an intravenous formulation for the treatment of acutely decompensated heart failure and in the outpatient setting as an oral formulation for the treatment of chronic heart failure.

*Market Opportunity.* Heart failure is a widespread and debilitating syndrome affecting millions of people in the United States. The high and rapidly growing prevalence of heart failure translates into significant hospitalization rates and associated societal costs. In 2004, 5.3 million patients carried a diagnosis of chronic heart failure in the United States. Many of these patients with chronic heart failure suffer acute episodes. The number of patients with diagnosed events of acute heart failure was over 4.1 million in 2004. These numbers are increasing due to the aging population and an increased likelihood of survival after acute myocardial infarction. The costs to society and the individual attributable to the prevalence of heart failure are high. The estimated annual direct and indirect costs of heart failure on the nation's health care system is estimated to be \$35 billion in 2008. A portion of that cost comes from heart failure drugs used to treat both chronic and acute heart failure. Sales of drugs to treat heart failure reached over \$1.6 billion in 2004, including \$1.3 billion for chronic heart failure and \$0.3 billion for acute heart failure. Despite currently available therapies, readmission rates for patients remain as high as high as 42% within one year of hospital discharge and mortality rates are approximately 60% over the five-year period following a diagnosis of chronic heart failure. The limited effectiveness of current therapies points to the need for next-generation therapeutics that may offer improved efficacy without increased adverse events.

Existing drugs that improve cardiac contractility, including milrinone, dobutamine and digoxin, treat heart failure in part by improving the contraction of cardiac cells, leading to an improvement in overall cardiac contractility. These drugs affect a complex cascade of cellular proteins, eventually resulting in an increase in intracellular calcium and a subsequent increase in cardiac cell contractility. However, activation of this cascade and the elevation of intracellular calcium levels may also impact other cardiac functions, producing unwanted and potentially life-threatening side effects, such as cardiac ischemia from increased oxygen demand and cardiac arrhythmias. Cardiac ischemia is a condition in which oxygen delivery to the heart is insufficient to meet the demand and is frequently observed in heart failure patients with ischemic cardiomyopathy due to atherosclerotic obstruction of blood vessels. Cardiac arrhythmias are irregularities in the frequency of the heart beat, to which heart failure patients are particularly susceptible even in the absence of drugs that may predispose to their occurrence. In addition, these existing drugs can cause vasodilation via their effects to relax vascular smooth muscle, leading to increases in heart rate and decreases in blood pressure which can complicate their use in this patient population. Therefore, although existing drugs that increase contractility may be effective in treating the symptoms of heart failure, they can increase heart failure patient morbidity and mortality.

*Our Approach.* We believe that the direct activation of cardiac myosin is a more specific mechanism by which to improve cardiac cell contractility. Cardiac myosin is the cytoskeletal protein in the cardiac cell that is directly responsible for converting chemical energy into the mechanical force that results in contraction. Cardiac muscle cell contractility is driven by the cardiac sarcomere, the fundamental unit of muscle contraction in the heart. The cardiac sarcomere is a highly ordered cytoskeletal structure composed of cardiac myosin, actin and a set of regulatory proteins. We believe that our cardiac myosin activators, such as CK-1827452, work through a novel mechanism of action that enables the modulation of cardiac cell contraction without increasing intracellular calcium levels or interfering with other unrelated cardiac muscle and vascular smooth muscle functions. Based on animal data and early stage clinical data in healthy volunteers, we believe that these compounds may effectively improve cardiac contractility and cardiac output for the treatment of heart failure patients without adversely impacting heart rate or

blood pressure and with only minimal effects on cardiac energy consumption. However, preclinical data on these compounds and clinical data on CK-1827452 in healthy volunteers may not be predictive of clinical results or adverse events in patients with heart failure. We are now conducting clinical testing with CK-1827452 in heart failure patients to evaluate its safety, tolerability, pharmacodynamics and pharmacokinetic profile for the potential treatment of this disease.

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We believe that our drug candidate CK-1827452 and other compounds from our cardiovascular program could be an improvement over existing heart failure drugs. Potential advantages of our cardiac myosin activators may include:

*Safety profile.* Our Phase I clinical trial of CK-1827452 administered intravenously to healthy volunteers indicated that, at the MTD, CK-1827452 enhanced cardiac pumping function, as evidenced by statistically significant increases in systolic ejection time, resulting in statistically significant increases in ejection fraction, stroke volume and fractional shortening, all without significantly increasing heart rate or causing cardiac arrhythmias. At intolerable doses, adverse effects appeared similar to the adverse findings observed in the preclinical safety studies, and occurred at similar plasma concentrations. These effects at intolerable doses are believed to be related to an excess of the intended pharmacologic effect and resolved promptly when administration of CK-1827452 ceased. These results are consistent with preclinical studies of CK-1827452 and our other cardiac myosin activators.

*Cardiac efficiency.* Our preclinical studies in animals with heart failure indicate that CK-1827452 and our other cardiac myosin activators enhance cardiac output, which is the volume of blood pumped into circulation by the heart per minute, and may improve cardiac efficiency, as measured by the ratio of cardiac work divided by cardiac oxygen consumption, where cardiac work is the product of cardiac output and blood pressure.

## ***Development Program***

Our clinical trials program for CK-1827452 is comprised of Phase I and Phase IIa trials designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of both intravenous and oral formulations CK-1827452 in a diversity of patients, including patients with stable heart failure and patients with ischemic cardiomyopathy. Our goal is to develop CK-1827452, in both intravenous and oral formulations, for the potential treatment of heart failure to be useful across the continuum of patient care, in both hospital and outpatient settings. Our Phase IIa clinical trials are intended to be designed to allow us to enroll a broad and representative population of heart failure patients in our planned Phase IIb and Phase III clinical trials.

Our current and recent clinical trials of CK-1827452 are as follows:

### **CK-1827452 (intravenous):**

*Phase I first-time-in-humans:* Clinical data for our first-time-in-humans Phase I clinical trial of CK-1827452, evaluating the safety, tolerability, pharmacodynamics and pharmacokinetic profile of a six-hour infusion of CK-1827452 in healthy volunteers were presented at the September 2006 Heart Failure Society of America Meeting. The maximum tolerated dose, or MTD, was 0.5 mg/kg/hr for this regimen. At this dose, the six-hour infusion of CK-1827452 produced statistically significant mean increases in left ventricular ejection fraction and fractional shortening of 6.8 and 9.2 absolute percentage points, respectively, as compared to placebo. These increases in indices of left ventricular function were associated with a mean prolongation of systolic ejection time of 84 milliseconds, which was also statistically significant. These mean changes in ejection fraction, fractional shortening and ejection time were concentration-dependent and CK-1827452 exhibited generally linear, dose-proportional pharmacokinetics across the range of doses studied. At the MTD, CK-1827452 was well-tolerated when compared to placebo. The adverse effects at the dose levels exceeding the MTD in humans appeared similar to the adverse findings observed in the preclinical safety studies, and occurred at similar plasma concentrations. These effects are believed to be related to an excess of the intended pharmacologic effect, resulting in excessive prolongation of the systolic ejection time, and resolved promptly with discontinuation of the infusions of CK-1827452. The Phase I clinical trial activity of CK-1827452 is consistent with results from preclinical models that evaluated CK-1827452 in normal dogs; however, further clinical trials are necessary to determine whether similar results will also be seen in patients with heart failure. A poster presented at the September 2007 Heart Failure Society of America Meeting provided additional data and

analysis regarding this trial. The objective of this analysis was to evaluate the concentration-response relationship of CK-1827452 on left ventricular function in healthy volunteers. The authors concluded that CK-1827452 increased left ventricular ejection fraction and left ventricular fractional shortening over a range of well-tolerated plasma concentrations. In addition, it was determined that systolic ejection time was the most sensitive marker of drug effect and that increases in left ventricular ejection fraction and left ventricular fractional shortening were well correlated with increases in systolic ejection

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time. Systolic ejection time is easily measured and we believe may serve as a useful indicator of this drug candidate's effect in patients with heart failure.

*Phase IIa stable heart failure:* In April 2007, we initiated a Phase IIa, multi-center, double-blind, randomized, placebo-controlled, dose-escalation clinical trial of CK-1827452 in patients with stable heart failure. The primary objective of this trial is to evaluate the safety and tolerability of CK-1827452 administered as an intravenous infusion to stable heart failure patients. The secondary objectives of this trial are to establish a relationship between the plasma concentration and pharmacodynamic effects of CK-1827452 and to determine the pharmacokinetics of CK-1827452 in stable heart failure patients. In addition to routine assessments of vital signs, blood samples and electrocardiographic monitoring, echocardiograms will be performed to evaluate cardiac function at various pre-defined time points. The clinical trial will consist of up to five cohorts of eight patients with stable heart failure. The first three of these cohorts will each undergo four treatment periods; patients will receive three escalating active doses of CK-1827452 administered intravenously and one placebo treatment which will be randomized into the dose escalation sequence. Patients in the fourth and fifth cohorts may receive only a single dose level of CK-1827452. In each cohort, patients will receive a one-hour loading infusion to rapidly achieve a target plasma concentration of CK-1827452, followed by a slower infusion intended to maintain that plasma concentration. These maintenance infusions are planned to be one hour in duration in the first two cohorts, and 23 hours in duration in the third cohort. We have completed the treatment phase for the second cohort of patients in this clinical trial. We anticipate interim data to be available from this trial in the first half of 2008. We anticipate final data to be available from this trial during the second half of 2008.

**CK-1827452 (oral)**

*Phase I oral bioavailability:* In December 2006, we announced results from a Phase I oral bioavailability study of CK-1827452 in healthy volunteers. This study was designed as an open-label, four-way crossover study in ten healthy volunteers designed to investigate the absolute bioavailability of two oral formulations (liquid and immediate-release solid formulations) of CK-1827452 versus an intravenous dose. In addition, the effect of taking the immediate-release solid formulation in a fed versus fasted state on the relative bioavailability of CK-1827452 was also assessed. Volunteers were administered, in random order, CK-1827452 at 0.125mg/kg as a liquid solution taken orally in a fasted state, an immediate-release solid formulation taken in fed and fasted states and a reference intravenous infusion at a constant rate over one hour. Pharmacokinetic data from this study demonstrated oral bioavailability of approximately 100% for each of the three conditions of oral administration. The median time to maximum plasma concentrations after dosing was 0.5 hours for the liquid solution taken orally, one hour for the immediate-release solid formulation taken in a fasted state, and three hours for the immediate-release solid formulation taken after eating. This rapid and essentially complete oral absorption suggests that predictable plasma levels can be achieved with chronic oral dosing in patients with heart failure. A poster summarizing the results of this study was presented at the September 2007 Heart Failure Society of America Meeting. The authors concluded that the near complete absolute bioavailability of CK-1827452 suggested that there is little or no first-pass metabolism of this drug candidate. In addition, food did not have a substantial effect on bioavailability but appeared to delay drug absorption in some subjects. CK-1827452, in both oral and intravenous formulations, was well-tolerated with no significant safety issues. We believe that these data support our current activities to develop a modified release oral formulation of CK-1827452 to enable late-stage clinical development of a dosing schedule that may be suitable for the treatment of patients with chronic heart failure.

*Phase I drug-drug interaction:* In April 2007, we announced the initiation of a single-center, open-label, sequential, parallel group, Phase I clinical trial of CK-1827452 designed to evaluate the effects of oral ketoconazole, a strong inhibitor of the metabolic enzyme cytochrome P450 (CYP) 3A4, on the pharmacokinetics of CK-1827452 given orally to up to 16 healthy male volunteers, 8 of whom have a normal genotype for CYP2D6, and up to 8 of whom have reduced CYP2D6 activity. In addition, the effects of diltiazem, a moderate CYP3A4 inhibitor, on the

pharmacokinetics of CK-1827452 will be assessed in 8 additional volunteers who are normal metabolizers by way of CYP2D6. We continue to enroll subjects with reduced CYP2D6 activity into this trial. We anticipate data from this trial to be available in 2008.

*Phase I multi-dose:* In July 2007, we announced the initiation of a single-center, Phase I clinical trial of CK-1827452 designed to evaluate the pharmacokinetics of an oral formulation of CK-1827452 in healthy volunteers. The trial progressed from a single-blind, single-dose phase to a randomized, double-blind, placebo-



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controlled, multi-dose phase. We completed treatment in this trial in December 2007. We anticipate data from this trial to be available in 2008.

*Phase I modified release:* In December 2007, we initiated a single-center, two-part, open-label, Phase I clinical trial of up to twelve healthy male volunteers. The primary objective of this trial is to assess the pharmacokinetics and relative bioavailability of three different oral modified release prototypes of CK-1827452. The secondary objective of the trial is to determine whether there is an effect of food on the pharmacokinetics on one of these oral modified release prototypes of CK-1827452. We anticipate data from this trial to be available in 2008.

### **2008 Planned Clinical Trials.**

In the first half of 2008, we anticipate initiating two additional Phase IIa clinical trials of CK-1827452. The first of these clinical trials is intended to evaluate an intravenous form of CK-1827452 in stable heart failure patients undergoing cardiac catheterization. The second is intended to evaluate an intravenous form together with an oral formulation of CK-1827452 in patients with ischemic cardiomyopathy.

*Amgen Strategic Alliance.* In December 2006, we entered into a collaboration and option agreement with Amgen to discover, develop and commercialize novel small-molecule therapeutics that activate cardiac muscle contractility for potential applications in the treatment of heart failure. In addition, the agreement granted Amgen an option to participate in future development and commercialization of CK-1827452 world-wide, except Japan. Under the agreement, in January 2007, Amgen made an upfront cash payment of \$42.0 million and a net equity investment of approximately \$32.9 million, which included a premium of \$6.9 million on the sale of equity. Cytokinetics and Amgen are performing joint research under the agreement focused on identifying and characterizing activators of cardiac myosin as back-up and follow-on potential drug candidates to CK-1827452. During the initial two-year research term, in addition to performing research at our own expense under the agreement, we will continue to conduct all development activities for CK-1827452, at our own expense, subject to Amgen's option and according to an agreed development plan. Amgen's option is exercisable at Amgen's election during a defined period, the ending of which is dependent upon the satisfaction of certain conditions, primarily the delivery of Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed development plan, the results of which may be sufficient to support its progression into Phase IIb clinical development. To exercise its option, Amgen would pay a non-refundable exercise fee of \$50.0 million and thereafter would be responsible for development and commercialization of CK-1827452 and related compounds, at its expense, subject to certain development and commercial participation rights of Cytokinetics. We may also be eligible under the agreement to receive pre-commercialization and commercialization milestone payments of up to \$600.0 million in the aggregate on CK-1827452 and other potential products arising from research under the collaboration, as well as royalties that escalate based on increasing levels of annual net sales of products commercialized under the agreement. The agreement also provides for us to receive increased royalties by co-funding Phase III development costs of drug candidates under the collaboration. If we elect to co-fund such costs, we would be allowed to co-promote products in North America and participate in agreed commercial activities in institutional care settings, at Amgen's expense. If Amgen elects not to exercise its option on CK-1827452, we may then independently proceed to develop CK-1827452 and the research collaboration would terminate.

*Commercialization.* If CK-1827452 or any of our other cardiac myosin activators receives regulatory approval, we expect to develop capabilities to market and sell the resulting drugs in North America for the treatment of acute heart failure. Because acute heart failure patients are largely treated in teaching and community-based hospitals that can be addressed by a specialized sales force, developing our commercial capabilities to address such treatment centers is consistent with our corporate strategy of focusing on large markets accessible by concentrated commercial efforts.

## **Oncology Program**

Our other major development program is focused on cancer, a disease of unregulated cell proliferation. Each of the anti-cancer drug candidates being developed under our sponsorship, namely ispinesib and SB-743921, is a structurally distinct small molecule that interferes with cell proliferation and promotes cancer cell death by specifically inhibiting kinesin spindle protein, or KSP. KSP is a mitotic kinesin that acts early in the process of cell division, or mitosis, during cell proliferation and is responsible for the formation of a functional mitotic spindle. Our

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third anti-cancer drug candidate, GSK-923295, is being developed under GSK's sponsorship and is directed against a second mitotic kinesin, centromere-associated protein E, or CENP-E. We initially discovered, characterized and optimized the various chemical series that led to ispinesib, SB-743921 and GSK-923295 in our research laboratories. All three of these drug candidates are being developed in connection with our strategic alliance with GSK. However, we have assumed responsibility for the conduct, at our expense, of the development of ispinesib and SB-743921, subject to GSK's option to resume responsibility for the development and commercialization for these drug candidates. We are conducting joint research directed to CENP-E in the seventh year of a research program under this strategic alliance. We are also researching other compounds for the potential treatment of cancer.

Ispinesib has been the subject of a broad Phase II clinical trials program conducted by GSK and the NCI designed to evaluate its efficacy against multiple tumor types. We believe that data from this ongoing clinical trials program has yielded a greater understanding of this drug candidate's clinical potential. We have reported Phase II clinical trial data for ispinesib in metastatic breast, non-small cell lung, ovarian, colorectal, head and neck, hepatocellular, renal and prostate cancers and in melanoma. To date, we believe clinical activity for ispinesib has been observed in non-small cell lung, ovarian and breast cancers, with the most robust clinical activity observed in a Phase II clinical trial evaluating ispinesib in the treatment of patients with locally advanced or metastatic breast cancer that had failed treatment with taxanes and anthracyclines. Under our strategic alliance with GSK, we have initiated, at our expense, a focused development program for ispinesib in the treatment of patients with locally advanced or metastatic breast cancer. This program is intended to build upon the previous data from the clinical trials conducted by GSK and the NCI, and is designed to further define the clinical activity profile of ispinesib in advanced breast cancer patients in preparation for potentially initiating a Phase III clinical trial of ispinesib for the second-line treatment of advanced breast cancer. In December 2007, we initiated a Phase I/II monotherapy clinical trial designed to evaluate ispinesib in the first-line treatment of chemotherapy-naïve patients with locally advanced or metastatic breast cancer on a more dose-dense schedule than was previously studied. We are conducting a Phase I/II trial of SB-743921 in Hodgkin and non-Hodgkin lymphoma on a similar more dose-dense schedule. In August 2007, we announced that GSK had initiated a first-time-in-humans Phase I clinical trial of GSK-923295 in patients with solid tumors.

*Market Opportunity.* Each year, over 1.4 million new patients are diagnosed with primary malignant solid tumors or hematological cancers in the United States. Five common cancer types – non-small cell lung, breast, ovarian, prostate and colorectal cancers – represented over 50% of all new cases of cancer in the United States each year and accounted for approximately 50% of all cancer deaths in the United States. Annually, over half a million people die from cancer. The prognosis for some types of cancer is more severe, such as non-small cell lung cancer, where the ratio of cancer-related deaths to newly diagnosed cases per year is approximately 75%.

The market for anti-cancer drugs in the United States in 2006 was estimated to be approximately \$18.1 billion. Within this market, we estimate that sales of drugs that inhibit mitosis, or anti-mitotic drugs, comprise a large portion of the commercial market for anti-cancer drugs. Taxanes, an important subset of anti-mitotic drugs, include paclitaxel from Bristol-Myers Squibb, or BMS, and docetaxel from Sanofi-Aventis Pharmaceuticals Inc., or Sanofi-Aventis. Sales in the United States of taxanes alone were estimated to be \$2.8 billion in 2006.

Since their introduction over 30 years ago, anti-mitotic drugs have advanced the treatment of cancer and are commonly used for the treatment of several tumor types. However, these drugs have demonstrated no treatment benefit against certain tumor types. In addition, these drugs target tubulin, a cytoskeletal protein that is essential not only to cell proliferation but also to other important cellular functions. The inhibition of these other cellular functions produces dose-limiting toxicities such as peripheral neuropathy, an impairment of the peripheral nervous system. Neuropathies result when these drugs interfere with the dynamics of microtubule filaments that are responsible for the long-distance transport of important cellular components within nerve cells.

*Our Approach.* Mitotic kinesins form a diverse family of cytoskeletal proteins that, like tubulin, facilitate the mechanical processes required for mitosis and cell proliferation. We have pharmaceutically characterized each of the 14 human mitotic kinesins that function in the pathway that enables mitosis. The first mitotic kinesin in this pathway, and the one upon which we have focused a majority of our research and development activities in this program, is KSP. Our drug candidates ispinesib and SB-743921 are KSP inhibitors. We have also engaged in research on a second mitotic kinesin, CENP-E. Our drug candidate GSK-923295 is a CENP-E inhibitor. We believe that drugs inhibiting KSP, CENP-E and other mitotic kinesins may represent the next generation of anti-mitotic

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drugs for the treatment of cancer. Mitotic kinesins are essential to mitosis and, unlike tubulin, appear to have no role in unrelated cellular functions and are expressed only in proliferating cells. We believe drugs that inhibit KSP, CENP-E and other mitotic kinesins may arrest mitosis and cell proliferation without significantly impacting unrelated, normal cellular functions, avoiding many of the toxicities commonly experienced by cancer patients treated with existing anti-mitotic drugs, and potentially overcoming cancer resistance mechanisms commonly seen with other marketed anti-mitotic drugs.

We believe our small molecule inhibitors of KSP and CENP-E are highly potent and specific. By inhibiting KSP, a cell cannot undertake the early steps of mitosis, the separation of the two poles of the mitotic spindle, which can result in cell death. In preclinical research, ispinesib and SB-743921, both KSP inhibitors, caused shrinkage of tumor size or reduction in tumor growth rates in more than ten different animal models. These preclinical models reveal favorable results for these drug candidates in comparison to existing drugs such as irinotecan, topotecan, gemcitabine, paclitaxel, vinblastine and cyclophosphamide. Alternatively, by inhibiting CENP-E, the dividing cell cannot proceed through the later stages of mitosis. These cells may then undergo cell death. In preclinical animal models of human cancer, GSK-923295 causes significant reductions in tumor size when administered as monotherapy.

We have identified, characterized and optimized several distinct structural classes of KSP and CENP-E inhibitors. We have also characterized several other mitotic kinesin inhibitors that may be researched further for their therapeutic potential. We believe that our anti-cancer drug candidates may be safer and, in certain tumor types, more effective than current anti-mitotic drugs.

Preclinical testing of ispinesib, SB-743921 and GSK-923295 and clinical trials of ispinesib and SB-743921 indicate that these drug candidates may have fewer toxicities than many existing anti-cancer drugs. Preclinical studies indicate that the primary toxicities are limited to gastrointestinal side effects and a reduction in bone marrow function. In clinical trials of ispinesib and SB-743921, the major dose-limiting toxicity was neutropenia, a decrease in the number of a certain type of white blood cell, which was generally reversible. We observed limited or no evidence of drug-related toxicities to the nervous system, heart, lung, kidney or liver. We believe that this safety profile could enable a higher therapeutic index for ispinesib and SB-743921 than for other anti-mitotics and potentially increase the therapeutic value of our two KSP inhibitors relative to other anti-mitotic drugs.

Preclinical testing also indicates that ispinesib, SB-743921 and GSK-923295 each cause tumor regression in the form of partial response, complete response or tumor growth inhibition in a variety of tumor types. This is consistent with the important role that mitotic kinesins play in cell proliferation in all tumor types. To date, we have observed clinical activity with ispinesib in metastatic breast, ovarian and non-small cell lung cancers. In addition, preclinical and Phase Ib clinical data on ispinesib indicate that it may have an additive effect when combined with existing chemotherapeutic agents.

## ***Development Program***

In 2007, we continued our development programs for ispinesib, SB-743921 and GSK-923295. Our most advanced drug candidate, ispinesib, continues to be tested in breast cancer, leukemia and pediatric solid tumors. We continue to conduct a Phase I/II clinical trial of SB-743921 in Hodgkin and non-Hodgkin lymphomas. GSK initiated a Phase I clinical trial for GSK-923295 in solid tumors in August 2007. We expect to announce data from these clinical trials throughout 2008.

## ***Ispinesib***

Ispinesib, our lead anti-cancer drug candidate, is a novel small molecule designed to inhibit cell proliferation and promote cancer cell death by specifically disrupting the function of KSP. The clinical trials program for ispinesib

conducted by GSK, in collaboration with the NCI, has been a broad program comprised of nine Phase II clinical trials and eight Phase I or Ib clinical trials evaluating the use of ispinesib in a variety of both solid and hematologic cancers. We believe that the breadth of this clinical trials program takes into consideration the potential and the complexity of developing a drug candidate such as ispinesib, and should help us to identify those tumor types and dosing regimens that are the most promising for the continued development of ispinesib. We have reported Phase II clinical trial data for ispinesib in metastatic breast, non-small cell lung, ovarian, colorectal, head and neck, hepatocellular, renal and prostate cancers and in melanoma. To date, we believe clinical activity for ispinesib has been observed in non-small cell lung, ovarian and breast cancers, with the most robust clinical activity observed in a Phase II clinical trial evaluating ispinesib in the treatment of patients with locally advanced or metastatic breast

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cancer that had failed treatment with taxanes and anthracyclines. In addition, GSK's Phase Ib clinical trials of ispinesib in combination with capecitabine, carboplatin and docetaxel demonstrated that ispinesib has an acceptable tolerability profile in combination with these standard chemotherapeutic agents. We are conducting a focused development program for ispinesib in the treatment of patients with locally advanced or metastatic breast cancer.

Currently ongoing and recently completed clinical trials of ispinesib are as follows:

*Breast Cancer:* In June 2007, we announced the final results from a multicenter Phase II clinical trial sponsored by GSK, which evaluated the safety and efficacy of ispinesib in the second- or third-line treatment of patients with locally advanced (Stage IIIB) or metastatic (Stage IV) breast cancer whose disease had recurred or progressed despite treatment with anthracyclines and taxanes. In this trial, patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The primary endpoint of the clinical trial was objective response as determined using the Response Evaluation Criteria in Solid Tumors, or RECIST. The best overall responses observed with ispinesib were partial responses in 4 of 45 evaluable patients as measured by RECIST and the duration of response ranged from 7.1 weeks to 30.0 weeks. The most common adverse event was Grade 4 neutropenia.

Based on these data and consistent with our focused approach to the further development of ispinesib, in December 2007, we initiated an open-label, non-randomized Phase I/II clinical trial designed to evaluate ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer. This trial is designed to be a proof-of-concept study to potentially amplify the signals of clinical activity seen in GSK's Phase II monotherapy trial of ispinesib in breast cancer, and is intended to provide the data necessary to inform ispinesib's further development, as well as to inform GSK's potential exercise of its option to develop and commercialize ispinesib. The Phase I portion of the Phase I/II trial is designed to determine the dose-limiting toxicity and MTD of ispinesib as monotherapy administered as a one-hour intravenous infusion on days 1 and 15 of a 28-day cycle in female patients with locally advanced or metastatic adenocarcinoma of the breast who have not received prior chemotherapy. Once an MTD is determined, the clinical trial is planned to move into Phase II, which is designed to assess the overall response rate of ispinesib in patients with measurable locally advanced or metastatic breast cancer who have not received prior chemotherapy, using RECIST. In the Phase II portion of this clinical trial, ispinesib is planned to be administered as a one-hour intravenous infusion on days 1 and 15 of a 28-day treatment cycle at the MTD determined in Phase I.

*Ovarian Cancer:* In June 2007 at the Annual Meeting of the American Society of Clinical Oncology, or ASCO, GSK presented data from Stage 1 of a two-stage Phase II trial of ispinesib as monotherapy in patients with platinum/taxane refractory or resistant relapsed ovarian cancer. The primary objective of this clinical trial was to evaluate the overall response rate with secondary objectives measuring the median time to radiographic response, median time to CA-125 response, median duration of radiographic response and progression-free survival. The best radiographic response was 1 partial response with a duration of 42 weeks and 5 patients with stable disease. Although a radiographic response was observed, none of the 22 evaluable patients had a CA-125 response and the median time to CA-125 progression was 5.3 weeks. In this clinical trial, the protocol-specific criteria to proceed to Stage 2 were not met. The most common adverse event was Grade 4 neutropenia.

*Renal Cell Cancer:* Included in the June 2007 ASCO proceedings was an abstract which presented interim data from a two-stage Phase II clinical trial of ispinesib in patients with advanced renal cell carcinoma sponsored by the NCI. The primary objective of this clinical trial was to assess overall response rate using RECIST. Secondary objectives included evaluating toxicities, time to progression and overall survival. In this clinical trial, 19 patients were enrolled and received ispinesib as monotherapy at 7 mg/m<sup>2</sup> as a one-hour infusion on days 1, 8 and 15 every 28 days with radiologic disease re-evaluation every 8 weeks. Of the 15 evaluable patients included in the interim analysis, the best response observed was stable disease in 7 patients after 8 weeks. One patient experienced Grade 3 neutropenia but no other Grade 3 or 4 toxicities were deemed to be attributable to the study drug. The authors concluded that treatment

with ispinesib as monotherapy at this dose and schedule in this patient population does not appear to lead to objective responses but appears to be well-tolerated.

*Prostate Cancer:* In June 2007, we announced results from Stage 1 of the NCI's two-stage, Phase II clinical trial for the treatment of patients with hormone refractory prostate cancer who had failed taxane-based chemotherapy, in which 21 patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. No patients met the primary endpoint of objective response as determined by blood levels of the tumor



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mass marker Prostate Specific Antigen or PSA and the median time to PSA or clinical progression was 9 weeks. Ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The most common adverse event was Grade 4 neutropenia.

*Hepatocellular Cancer:* In June 2007, we announced the results from Stage 1 of the NCI's two-stage, Phase II clinical trial for the treatment of hepatocellular cancer, in which 15 patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The best overall response was stable disease seen in 7 of the 15 patients. Ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The most common adverse event was Grade 4 neutropenia.

*Melanoma:* In June 2007, we announced the results from Stage 1 of the NCI's two-stage, Phase II clinical trial for the treatment of patients with chemotherapy-naïve recurrent or metastatic malignant melanoma, in which 17 patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The best overall response was stable disease seen in 6 of 17 patients treated. Ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The most frequent Grade 3 or 4 hematologic adverse events were neutropenia and lymphopenia.

*Ispinesib with capecitabine.* In the second quarter of 2007, GSK concluded patient treatment in a dose-escalating, Phase Ib clinical trial evaluating the safety, tolerability and pharmacokinetic profile of ispinesib in combination with capecitabine. In 2006, interim clinical trial data were presented demonstrating that the combination of ispinesib and capecitabine may have an acceptable tolerability profile. The optimally tolerated regimen in this clinical trial was not defined at that time; however, the MTD of ispinesib as monotherapy (18 mg/m<sup>2</sup>, administered as an intravenous infusion every 21 days) was tolerated with therapeutic doses of capecitabine, specifically daily oral doses of 2000 mg/m<sup>2</sup> and 2500 mg/m<sup>2</sup> for 14 days. Plasma concentrations of ispinesib did not appear to be affected by the presence of capecitabine. Dose-limiting toxicities consisted of Grade 2 rash that did not allow 75% of the capecitabine doses to be delivered and prolonged Grade 4 neutropenia. In this clinical trial, a total of 12 out of 24 patients had a best response of stable disease as determined by RECIST. We anticipate final data from this clinical trial to be available in the first half of 2008. The timing of availability of these data is based on information provided by GSK and is outside of our control.

*Pediatric Solid Tumors:* The NCI continues to conduct a Phase I clinical trial designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of ispinesib as monotherapy administered as a one-hour infusion on days 1, 8 and 15 of a 28-day schedule to pediatric patients with relapsed or refractory solid tumors.

*Acute Leukemias, Chronic Myelogenous Leukemia or Advanced Myelodysplastic Syndromes:* The NCI has closed enrollment in a Phase I clinical trial designed to evaluate the safety, tolerability and pharmacokinetic profile of ispinesib as monotherapy administered as a one-hour infusion on days 1, 2 and 3 of a 21-day cycle to adult patients with relapsed or refractory acute leukemias, chronic myelogenous leukemia in blast crisis or advanced myelodysplastic syndromes.

*Preclinical Research:* At the 2007 Annual Meeting of the American Association for Cancer Research, or AACR, a poster was presented containing data from non-clinical studies designed to examine whether spindle disruption by inhibition of KSP with ispinesib may have therapeutic potential in the treatment of multiple myeloma. The authors concluded that KSP inhibition with ispinesib was able to induce growth arrest and cell death in myeloma cells, and overcome resistance to both conventional drugs and novel agents, such as bortezomib. They also concluded that ispinesib's preferential activity against transformed plasma cells with the sparing of normal bone marrow cells provides a rationale for the clinical development of ispinesib as a potential treatment for relapsed or refractory multiple myeloma.

SB-743921

SB-743921, our second anti-cancer drug candidate, also inhibits KSP but is structurally distinct from ispinesib. SB-743921 is also being developed in connection with our strategic alliance with GSK. Though we are aware of no clinical shortcomings of ispinesib that are addressed by SB-743921, we believe that having two KSP inhibitors in concurrent clinical development increases the likelihood that a commercial product will result from this research and development program.

SB-743921 was studied by GSK in a dose-escalating Phase I clinical trial evaluating its safety, tolerability and pharmacokinetics in advanced cancer patients. The primary objectives of this clinical trial were to determine the

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dose limiting toxicities, or DLTs, and to establish the MTD of SB-743921 administered intravenously on a once every 21-day schedule. Secondary objectives included assessment of the safety and tolerability of SB-743921, characterization of the pharmacokinetics of SB-743921 on this schedule and a preliminary assessment of its anti-tumor activity. The observed toxicities at the recommended Phase II dose were manageable. DLTs in this clinical trial consisted predominantly of neutropenia and elevations in hepatic enzymes and bilirubin. Disease stabilization, ranging from 9 to 45 weeks, was observed in seven patients. One patient with cholangiocarcinoma had a confirmed partial response at the MTD.

In 2006, we initiated, at our expense, an additional clinical trial of SB-743921 in hematologic cancers. We continue to enroll and dose-escalate patients in this open-label, non-randomized Phase I/II clinical trial to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of SB-743921 administered as a one-hour infusion on days 1 and 15 of a 28-day schedule in patients with Hodgkin or non-Hodgkin lymphoma. In December 2007, at the Annual Meeting of the American Society of Hematology, a poster was presented summarizing interim data from Phase I of this clinical trial. The authors concluded that SB-743921 is well-tolerated without prophylactic granulocyte-colony stimulating factor at doses less than 6 mg/m<sup>2</sup> when given on this alternative dosing schedule. The best response observed was a partial response in a patient with Hodgkin lymphoma at 6 mg/m<sup>2</sup>. In this interim analysis, Grade 3 or 4 neutropenia was the most common toxicity reported and Grade 3 or 4 non-hematological toxicities have been rare. In particular, there has been no evidence of neuropathy. We anticipate final data to be available from the Phase I portion of this trial in the first half of 2008.

## **GSK-923295**

GSK-923295 is the third drug candidate to arise from our strategic alliance with GSK. GSK-923295 is an inhibitor of a second mitotic kinesin, CENP-E. CENP-E is directly involved in coordinating the decision a cell makes to divide with the actual trigger of the mechanics of cell division. These processes are essential for cancer cells to grow. GSK-923295 causes partial and complete shrinkages of human tumors in animal models and has exhibited properties in these studies that distinguish it from ispinesib and SB-743921.

In August 2007, we announced that GSK had initiated a first-time-in-humans Phase I clinical trial of GSK-923295. This Phase I clinical trial is an open-label, non-randomized, dose-finding trial designed to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of GSK-923295 in patients with advanced solid tumors. The initiation of this clinical trial triggered a milestone payment of \$1.0 million from GSK to Cytokinetics under the GSK Agreement. We anticipate data to be available from this clinical trial in 2008. The timing of availability of these data is based on information provided by GSK and is outside of our control.

Preclinical data relating to GSK-923295 were presented in two posters at the 2007 AACR Meeting. The authors of one poster concluded that GSK-923295, a potent and selective inhibitor of CENP-E, elicited a dose-dependent response against a wide variety of human tumor xenografts models in nude mice. Tumor regression was observed in seven of eleven of the models studied. The mechanism of cell cycle arrest was consistent with that observed in cell culture, as judged by histological examination of tumors in a colon cancer xenograft. The authors of the second poster, a biochemical analysis of GSK-923295, described its unique mechanism of CENP-E inhibition. This biochemical mechanism of action is consistent with the cellular response and clearly distinguishable from the mitotic kinesin inhibitors ispinesib and monastrol.

In October 2007, at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, two posters related to GSK-923295 were presented. The first poster described the antiproliferative activity of GSK-923295 across a panel of 214 solid and 85 hematological tumor cell lines. Activity was not limited to any one tumor type and only four of the cell lines tested were fully resistant to treatment with our CENP-E inhibitor. In a second poster, the molecular basis for response to GSK-923295 was characterized across a series of cell lines with

varying sensitivity and related to the mitotic checkpoint and programmed cell death machinery.

*GSK Strategic Alliance.* Ispinesib, SB-743921 and GSK-923295 are being developed in connection with the GSK Agreement, executed in 2001. This strategic alliance is directed to the discovery, development and commercialization of novel small molecule drugs targeting KSP, CENP-E and certain other mitotic kinesins for applications in the treatment of cancer and other diseases. Under our strategic alliance, GSK, in collaboration with the NCI, conducted a broad Phase II clinical trials program designed to evaluate ispinesib across multiple tumor types, as well as a Phase I clinical trial of SB-743921. GSK is currently conducting a Phase I clinical trial of

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GSK-923295. We will receive royalties from GSK's sales of any drugs developed under the strategic alliance. For those drug candidates that GSK develops under the strategic alliance, we can elect to co-fund certain later-stage development activities which would increase our potential royalty rates on sales of resulting drugs and provide us with the option to secure co-promotion rights in North America. If we elect to co-fund later-stage development, we expect that the royalties to be paid on future sales of each of ispinesib, SB-743921 and GSK-923295 could potentially increase to an upper-teen percentage rate based on increasing product sales and our anticipated level of co-funding. If we exercise our co-promotion option, then we are entitled to receive reimbursement from GSK for certain sales force costs we incur in support of our commercial activities.

In November 2006, we amended the GSK Agreement and assumed responsibility, at our expense, for the continued research, development and commercialization of inhibitors of KSP, including ispinesib and SB-743921, and other mitotic kinesins, other than CENP-E which is the focus of translational research activities being conducted by GSK and Cytokinetics and development activities being conducted by GSK. The November 2006 amendment supersedes a previous amendment to the agreement dated September 2005, which specifically related to SB-743921. In each of June 2006 and June 2007, we amended the GSK Agreement to extend the research term of this strategic alliance for an additional year to continue activities focused towards translational research directed to CENP-E.

Under the November 2006 amendment, our development of ispinesib and SB-743921 is subject to GSK's option to resume responsibility for the development and commercialization of either or both drug candidates during a defined period. If GSK exercises its option for a drug candidate, it will pay us an option fee equal to the costs we independently incurred for that drug candidate, plus a premium intended to compensate us for the cost of capital associated with such costs, subject to an agreed limit for such costs and premium. Upon GSK exercising its option for a drug candidate, we may receive additional pre-commercialization milestone payments with respect to such drug candidate and increased royalties on net sales of any resulting product, in each case, beyond those contemplated under the original agreement. If GSK does not exercise its option for either ispinesib or SB-743921, we will be obligated to pay royalties to GSK on the sales of any resulting products. Under the amended strategic alliance, we intend to conduct a focused development program for ispinesib in the treatment of patients with locally advanced or metastatic breast cancer. This program is intended to build upon the previous data from the clinical trials conducted by GSK and the NCI, and would be designed to further define the clinical activity profile of ispinesib in advanced breast cancer patients in preparation for potentially initiating a Phase III clinical trial of ispinesib for the second-line treatment of advanced breast cancer. As part of this development program, in December 2007, we initiated an open-label, non-randomized Phase I/II clinical trial designed to evaluate ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer. We are continuing to conduct a Phase I/II clinical trial of SB-743921 for Hodgkin and non-Hodgkin lymphoma.

In August 2007, we announced that GSK had initiated a first-time-in-humans Phase I clinical trial of GSK-923295 in patients with advanced solid tumors. The initiation of this clinical trial triggered a milestone payment of \$1.0 million from GSK to us under the GSK Agreement.

*Commercialization.* We expect to develop sales and marketing capabilities to support the North American commercialization of one or more of ispinesib, SB-743921, GSK-923295 and other drug candidates that may be developed under our strategic alliance with GSK. Because cancer patients are largely treated in institutional and other settings that can be addressed by a specialized sales force, developing our commercial capabilities to address such treatment centers is consistent with our corporate strategy of focusing our commercial efforts on large, concentrated markets.

## **Discovery Programs**

Our drug discovery platform primarily has been based on our advanced understanding of the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. The cytoskeleton is one of a few biological areas with broad potential for drug discovery and development and has been scientifically and commercially validated in a wide variety of human diseases. For example, a cytoskeletal structure in the cardiac muscle cell called the cardiac sarcomere plays a fundamental role in cardiac contraction. Heart failure is a syndrome often caused by reduced cardiac contractility. Our activities in this area have led to the discovery and development of our drug candidate CK-1827452 for the potential treatment of heart failure, and we have continued to discover

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and develop other small molecules that increase cardiac contractility as back-up compounds for this program. The cytoskeleton also plays a fundamental role in cell proliferation, and cancer is a disease of unregulated cell proliferation. Hence, small molecule inhibitors of these cytoskeletal proteins may prevent cancer cells from proliferating. Our activities in this area have led to the discovery and development of our current drug candidates ispinesib, SB-743921 and GSK-923295 for the potential treatment of cancer, and we have continued to discover other compounds targeting the cytoskeleton that may also be useful for the treatment of cancer.

Currently, we are conducting drug discovery activities on several earlier stage research programs that we believe will continue to contribute novel drug candidates to our pipeline over time. In each case, our decision to pursue these programs is based on a therapeutic rationale regarding the role of specific cytoskeletal proteins implicated in the relevant disease and desired treatment. In each of these areas, our research activities are directed towards the modulation of a specific cytoskeletal protein pathway or multi-protein system for the treatment of disease. For example, in our muscle biology research programs, we have identified, characterized and chemically optimized compounds that inhibit or activate selectively the cytoskeletal structure involved in the contraction of smooth or skeletal muscle cells, respectively. Our objective for these research programs is to discover potential drug candidates for the potential treatment of high blood pressure, bronchoconstriction and diseases related to skeletal muscle deficits. We have evaluated certain of these compounds in animal models for the potential treatment of hypertension, a disease in which elevated blood pressure may be decreased by relaxation of the arterial smooth muscle; asthma, a disease in which constriction of the airways may be decreased by relaxation of the pulmonary smooth muscle; and neuromuscular diseases which may be subject to treatment through increasing the contractility of skeletal muscle. In 2008, we anticipate that at least one additional potential drug candidate from our current lead compound optimization activities directed to smooth or skeletal muscle contractility will advance into studies designed to support the regulatory filings necessary to initiate first-time-in-humans clinical trials. We believe that we may be able to strategically partner compounds from either or both of our skeletal muscle contractility and smooth muscle contractility programs. In addition, our proprietary technologies created through our experience in the mechanics and regulation of cell cycle progression has enabled the discovery of compounds that may have a unique mechanism for inhibiting cell proliferation, and may have future application for the treatment of cancer.

All of our drug candidates and potential drug candidates were discovered by leveraging our drug discovery expertise focused on cytoskeletal pharmacology. We believe that our knowledge of the cytoskeleton enables us to develop novel and potentially safer and more effective classes of drugs directed at the treatment of cardiovascular diseases, cancer and other diseases. We have developed a cell biology driven approach and proprietary technologies to evaluate the function of many interacting proteins in the complex environment of the intact human cell. This approach, which we applied initially to the cytoskeleton and are now expanding to other areas of cell biology, enables increased speed, efficiency and yield not only in our drug discovery process, but also potentially in clinical development. We focus on developing a detailed understanding of validated protein pathways and multi-protein systems to allow our assay systems to more correctly represent the natural environment of a human cell. This approach differs from the conventional practice of concentrating on individual protein targets assayed in a system that may not adequately represent the complex, dynamic and variable natural environment that is relevant to disease. As a result, we can potentially identify multiple points of biological intervention to modulate a specific protein pathway or multi-protein system. Our discovery activities are thus directed at particular proteins and biological pathways that may be better targets for the development of potentially safer and more effective drugs. We expect to continue to identify additional potential drug candidates that may be suitable for clinical development.

Our PUMA™ system and Cytometrix® technologies enable early identification and prioritization of compounds that are highly selective for their intended protein targets without other cellular effects, and may thereby be less likely to give rise to clinical side effects. The integrated use of these technologies enables us to efficiently focus our activities towards those compounds directed at novel protein targets that are more likely to yield attractive drug candidates. Our PUMA™ system is a high-throughput screening platform comprised of a series of automated proprietary multi-protein

biochemical assays designed to comprehensively screen large compound libraries to yield chemical entities that specifically modulate each of several molecular motor proteins. Unlike many screening platforms, these technologies allow us to analyze protein pathway activity and complexity in a high-throughput format that we believe is more predictive of the natural cellular environment. Application of our Cytometrix® technologies to small molecules identified in this way allows us to identify quickly compounds that elicit the appropriate cellular response without other effects and thereby more likely achieve a desired therapeutic effect.



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Cytometrix® technologies are our proprietary suite of automated and digital microscopy assays and analytical software that enable us to screen for potency, efficacy and specificity against multiple biological targets in cells, facilitating the early identification and rejection of those compounds that may have unintended effects and that may subsequently give rise to toxicities. Cytometrix® technologies systematically and comprehensively measure responses of individual human cells to potential drug candidates across multiple experimental conditions. For example, in our cardiovascular program, Cytometrix® technologies are used to examine the detailed response of cardiac cells to our small molecules that affect contractility of these cells. In our oncology program, Cytometrix® technologies measure, on a cell-by-cell basis, the number of cells at each stage of cell division with a high degree of resolution. As an adjunct to all of our drug discovery programs, we have developed a Cytometrix® module to identify small molecules with undesired effects in liver cells. Often, such undesired effects can cause small molecules to fail during the course of development. By understanding the potential for such a liability early, our small molecule optimization programs can be directed to minimize the undesired effect. Through the integrated use of our PUMAtm system and Cytometrix® technologies, we believe that we are able to efficiently focus our activities towards those compounds that are specifically directed towards novel protein targets and that are more likely to yield attractive drug candidates.

*AstraZeneca Strategic Alliance.* In December 2003, we formed a strategic alliance with AstraZeneca to develop automated imaging-based cellular phenotyping and analysis technologies for the in vitro prediction of hepatotoxicity, or toxicity of the liver, a common reason that drug candidates fail in preclinical and clinical development. Under our collaboration and license agreement, AstraZeneca committed to reimburse us for full-time employee equivalents, or FTEs, in our technology department over the two-year research term, pay annual licensing fees and make a milestone payment to us upon the successful achievement of certain agreed-upon performance criteria. These performance criteria were not met. The research term of the agreement with AstraZeneca expired in December 2005, and we formally terminated the agreement in August 2006.

## **The Cytoskeleton**

The cytoskeleton is a diverse, multi-protein framework that carries out fundamental mechanical activities of cells including mitosis, or the division of genetic material during cell division, intracellular transport, cell movement and contraction and overall cell organization. It provides an ordered and dynamic organizational scaffolding for the cell, and mediates movement, whether of proteins within the cell or of the entire cell itself. The cytoskeleton is comprised of a unique set of filaments and molecular motor proteins. Filaments are long linear structures of proteins that serve as the major scaffolding in cells and conduits for movement of molecular motor proteins transporting other proteins or intracellular material. Microtubule filaments are composed of tubulin, and actin filaments are composed of actin. Molecular motor proteins, such as kinesins and myosins, are proteins that transport materials within cells and are also responsible for cellular movement. Kinesins move along microtubule filaments and myosins move along actin filaments.

Cytoskeletal proteins organize into ordered protein pathways or multi-protein systems that perform important cellular functions. For example, a multi-protein cytoskeletal structure, called the cardiac sarcomere, contains a highly ordered array of cardiac myosin interacting with actin filaments. The movement of myosin along actin filaments generates the cell contraction responsible for cardiac muscle function. Our program in heart failure is focused on discovering potential drugs that activate cardiac myosin. One of our founders and scientific advisory board members, Dr. James Spudich, was one of the first scientists to characterize the functional interrelationships of the cytoskeletal proteins in the sarcomere.

Another cytoskeletal structure called the mitotic spindle organizes and divides genetic material during cell proliferation. The mitotic spindle encompasses many cytoskeletal proteins including tubulin, which forms microtubule filaments, and a sub-group of kinesins known as mitotic kinesins. The highly orchestrated action of the proteins within this structure transports and segregates genetic material during cell proliferation. Our most advanced cancer program,

partnered with GSK, is focused on discovering potential drugs that inhibit human mitotic kinesins. One of our founders and scientific advisory board members, Dr. Ron Vale, first discovered kinesins. Another of our founders and scientific advisory board members, Dr. Larry Goldstein, was the first scientist to identify and characterize kinesin genes.

Beyond the role these specific cytoskeletal proteins play in cardiac muscle contraction and cell proliferation, other cytoskeletal proteins have been implicated in a variety of other important biological processes and related

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human diseases. Our drug discovery activities are focused on several of these mechanical cellular processes, including cell proliferation and cardiac and other muscle contraction, and are specifically directed at the cytoskeletal proteins that play essential roles in carrying out these functions. For instance, in our muscle biology research programs, we have identified, characterized and are now seeking to chemically optimize compounds that inhibit or activate selectively the cytoskeletal structure involved in the contraction of smooth or skeletal muscle cells, respectively. We are evaluating certain of these compounds in animal models for the potential treatment of hypertension, a disease in which elevated blood pressure may be decreased by relaxation of the arterial smooth muscle; asthma, a disease in which constriction of the airways may be decreased by relaxation of the pulmonary smooth muscle; and neuromuscular diseases which may be subject to treatment through increasing the contractility of skeletal muscle.

## **Our Patents and Other Intellectual Property**

Our policy is to patent the technology, inventions and improvements that we consider important to the development of our business. As of December 31, 2007, we had 119 issued United States patents and over 100 additional pending United States and foreign patent applications. In addition, we have an exclusive license to 15 United States patents and a number of pending United States and foreign patent applications from the University of California and Stanford University. We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive position.

We seek to protect our proprietary information by requiring our employees, consultants, contractors, partners and other advisers to execute nondisclosure and invention assignment agreements upon commencement of their employment or engagement, through which we seek to protect our intellectual property. Agreements with our employees also prevent them from bringing the proprietary information or materials of third parties to us. We also require confidentiality agreements or material transfer agreements from third parties that receive our confidential information or materials.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for 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 from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent positions of pharmaceutical, biotechnology and other 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 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 and 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.

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

we or our licensors might not have been the first to make the inventions covered by each of our 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 or 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 that are patentable; or

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the patents of others may prevent or limit our ability to conduct our business.

The defense and prosecution of intellectual property suits, interferences, oppositions and related legal and administrative proceedings in the United States are costly, time consuming to pursue and result in diversion of resources. The outcome of these proceedings is uncertain and could significantly harm our business.

We also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, partners and other advisors may unintentionally or willfully disclose our trade secrets to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets would be expensive and time consuming, and the outcome would be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop information that is equivalent to our trade secrets.

The pharmaceutical, biotechnology and other life sciences industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. As our drug candidates progress toward commercialization, the possibility of an infringement claim against us increases. While we attempt to ensure that our drug candidates and the methods we employ to manufacture them do not infringe other parties' patents and other proprietary rights, competitors or other parties may still assert that we infringe on their proprietary rights.

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 U.S. patent claims a method of use for inhibiting signaling by what is called the hedgehog pathway using certain such compounds. Curis also 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. One of the European patents which we opposed was recently revoked and is no longer valid in Europe. Curis has appealed this decision. Curis or a third party may assert that the sale of isspinesib may infringe one or more of these 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 any additional oppositions would be successful. We have not attempted to obtain a license to these patents. 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.

## **Government Regulation**

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture, marketing and distribution of drugs. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, labeling, storage, record keeping, approval, advertising and promotion of our drug candidates and drugs.

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act and implementing regulations. The process required by the FDA before our drug candidates may be marketed in the United States generally involves the following:

completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies, all performed in accordance with the FDA's good laboratory practice, or GLP, regulations;

submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical trials may begin;

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performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;

submission of a new drug application, or NDA, to the FDA;

satisfactory completion of an FDA preapproval inspection of the manufacturing facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, regulations; and

FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

This testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our drug candidates will be granted on a timely basis, if at all.

Preclinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of preclinical tests, together with manufacturing information and analytical data, are submitted as part of an IND application to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Similar regulatory procedures generally apply in those countries outside of the United States where we conduct clinical trials. Our submission of an IND or a foreign equivalent, or those of our collaborators, may not result in authorization from the FDA or its foreign equivalent to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, or its foreign equivalent, for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the clinical trial until completed. The FDA or its foreign equivalent, the IRB or its foreign equivalent, or the clinical trial sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive good clinical practice, or GCP, regulations and regulations for informed consent.

*Clinical Trials:* For purposes of an NDA submission and approval, clinical trials are typically conducted in the following three sequential phases, which may overlap:

*Phase I:* The clinical trials are initially conducted in a limited population to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients, such as cancer patients. In some cases, particularly in cancer trials, a sponsor may decide to run what is referred to as a Phase Ib clinical trial, which is a second, safety-focused Phase I trial typically designed to evaluate the impact of the drug candidate in combination with currently approved drugs.

*Phase II:* These clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, to make an initial determination of potential efficacy of the drug candidate for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase III clinical trials. Phase IIa clinical trials generally are designed to study the pharmacokinetic or pharmacodynamic properties and conduct a preliminary assessment of safety of the drug candidate over a measured dose response range. In some cases, a sponsor may decide to run what is referred to as a Phase IIb clinical trial, which is a second, typically larger, confirmatory Phase II trial that could, if positive and accepted by the FDA, serve as a pilot or pivotal clinical trial in the approval of a drug candidate.

*Phase III:* These clinical trials are commonly referred to as pivotal clinical trials. If the Phase II clinical trials demonstrate that a dose range of the drug candidate is effective and has an acceptable safety profile, Phase III clinical trials are then undertaken in large patient populations to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites.

In some cases, the FDA may condition approval of an NDA for a drug candidate on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase IV clinical trials. Additionally, the Food and Drug Amendments Act of 2007 requires that all clinical trials we conduct for our drug candidates, both before and after approval, and the



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results of those trials, be included in a clinical trials registry database that is available and accessible to the public via the internet. Our failure to properly participate in the clinical trial database registry would subject us to significant civil monetary penalties.

*New Drug Application.* The results of drug candidate development, preclinical testing and clinical trials are submitted to the FDA as part of an NDA. The NDA also must contain extensive manufacturing information. Once the submission has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of an NDA if the applicable regulatory criteria are not satisfied, or it may require additional clinical data, including data in a pediatric population, or an additional pivotal Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we or our collaborators do. Once issued, the FDA may withdraw a drug approval if ongoing regulatory requirements are not met or if safety problems occur after the drug reaches the market. In addition, the FDA may require further testing, including Phase IV clinical trials, and surveillance or restrictive distribution programs to monitor the effect of approved drugs which have been commercialized. The FDA has the power to prevent or limit further marketing of a drug based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to a drug, including changes in indications, labeling or manufacturing processes or facilities, we may be required to submit and obtain prior FDA approval of a new NDA or NDA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

*Fast Track Designation.* The FDA's fast track program is intended to facilitate the development and to expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug candidate may request the FDA to designate the drug candidate for a specific indication as a fast track drug concurrent with or after the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request.

If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the time period specified in the Prescription Drug User Fees Act, which governs the time period goals the FDA has committed to reviewing an application, does not begin until the complete application is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

In some cases, a fast track designated drug candidate may also qualify for one or more of the following programs:

*Priority Review.* Under FDA policies, a drug candidate is eligible for priority review, or review within a six-month time frame from the time a complete NDA is accepted for filing, if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. A fast track designated drug candidate would ordinarily meet the FDA's criteria for priority review. We cannot guarantee any of our drug candidates will receive a priority review designation, or if a priority designation is received, that review or approval will be faster than conventional FDA procedures, or that FDA will ultimately grant drug approval.

*Accelerated Approval.* Under the FDA's accelerated approval regulations, the FDA is authorized to approve drug candidates that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses, and that provide meaningful therapeutic benefit to patients over existing treatments based upon either a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than patient survival. In clinical trials, surrogate endpoints are

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alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable clinical symptoms. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase IV or post-approval clinical trials to validate the surrogate endpoint or confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to validate a surrogate endpoint or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

When appropriate, we and our collaborators intend to seek fast track designation or accelerated approval for our drug candidates. We cannot predict whether any of our drug candidates will obtain a fast track or a priority review designation, or the ultimate impact, if any, of the fast track or a priority review process on the timing or likelihood of FDA approval of any of our drug candidates.

Satisfaction of FDA regulations and requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Typically, if a drug candidate is intended to treat a chronic disease, as is the case with some of our drug candidates, safety and efficacy data must be gathered over an extended period of time. Government regulation may delay or prevent marketing of drug candidates for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our drug candidates on a timely basis, if at all. Even if a drug candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages or restrictive distribution programs. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a drug may result in restrictions on the drug or even complete withdrawal of the drug from the market. Delays in obtaining, or failures to obtain, regulatory approvals for any of our drug candidates would harm our business. In addition, we cannot predict what adverse governmental regulations may arise from future United States or foreign governmental action.

*Other regulatory requirements.* Any drugs manufactured or distributed by us or our collaborators pursuant to FDA approvals are subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications

regarding off-label use.

**Competition**

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address cardiovascular diseases and cancer, each of which is highly competitive. We face significant competition from most pharmaceutical companies as well as biotechnology companies that are also researching and selling products

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designed to address cardiovascular diseases and cancer. Many of our competitors have significantly greater financial, manufacturing, marketing and drug development resources than we do. Large pharmaceutical companies in particular have extensive experience in clinical testing and in obtaining regulatory approvals for drugs. These companies also have significantly greater research capabilities than we do. In addition, many universities and private and public research institutes are active in research of cardiovascular diseases and cancer, some in direct competition with us.

We believe that our ability to successfully compete will depend on, among other things:

- our drug candidates' efficacy, safety and reliability;
- the speed and cost-effectiveness at which we develop our drug candidates;
- the successful completion of clinical development and laboratory testing and our success in obtaining regulatory approvals for drug candidates;
- the timing and scope of regulatory approvals for our drug candidates;
- our ability to manufacture and sell commercial quantities of a drug to the market;
- acceptance of our drugs by physicians and other health care providers;
- the willingness of third party payors to provide reimbursement for the use of our drugs;
- our ability to protect our intellectual property and avoid infringing the intellectual property of others;
- the quality and breadth of our technology;
- our employees' skills and our ability to recruit and retain skilled employees;
- our cash flows under existing and potential future arrangements with licensees, partners and other parties; and
- the availability of substantial capital resources to fund development and commercialization activities.

Our competitors may develop drug candidates and market drugs that are less expensive and more effective than our future drugs or that may render our drugs obsolete. Our competitors may also commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates.

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 branded drugs such as nesiritide, as well as potentially against other novel drug candidates in development such as urocortin II, which is being developed by Neurocrine Biosciences, Inc., or Neurocrine; ularitide, which is being developed by PDL BioPharma, Inc., or PDL; CD-NP, which is being developed by Nile Therapeutics, Inc., or Nile; and levosimendan, which is being developed in the United States by Abbott Laboratories, or Abbott, in collaboration with Orion Pharma, or Orion, and is commercially available in a number of countries outside of the United States.

If approved for marketing by the FDA, depending on the approved clinical indication, our anti-cancer drug candidates such as ispinesib and SB-743921 and our potential drug candidate GSK-923295 could compete against existing cancer treatments such as paclitaxel and its generic equivalents, docetaxel, vincristine, vinorelbine, navelbine, ixabepilone and potentially against other novel anti-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, BMS, Array, Lilly, Arqule and others are conducting research and development focused on KSP and other mitotic kinesins. In addition, BMS, Merck, Novartis, Genentech, Inc., AstraZeneca, Kosan Biosciences Incorporated, or Kosan, Hoffman-La Roche Ltd., or Roche, and other pharmaceutical and biopharmaceutical companies are developing other approaches to inhibiting mitosis.

Other companies that are early-stage are currently developing alternative treatments and products that could compete with our drugs. These organizations also compete with us to attract qualified personnel and potential parties for acquisitions, joint ventures or other strategic alliances.

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### **Employees**

As of December 31, 2007, our workforce consisted of 161 full-time employees, 47 of whom hold Ph.D. or M.D. degrees, or both, and 33 of whom hold other advanced degrees. Of our total workforce, 123 are engaged in research and development and 38 are engaged in business development, finance and administration functions. We have no collective bargaining agreements with our employees, and we have not experienced any work stoppages. We believe that our relations with our employees are good.

### **Available Information**

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is <http://www.sec.gov>.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website on the World Wide Web at <http://www.cytokinetics.com> or by contacting the Investor Relations Department at our corporate offices by calling 650-624-3000.

### **Item 1A. Risk Factors**

*In evaluating our business, you should carefully consider the following risks in addition to the other information in this report. Any of the following risks could materially and adversely affect our business, results of operations, financial condition or your investment in our securities, and many are beyond our control. It is not possible to predict or identify all such factors and, therefore, you should not consider any of the above risks to be a complete statement of all the potential risks or uncertainties that we face.*

#### **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 or are significantly delayed 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 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. CK-1827452, our drug candidate for the treatment of heart failure, and ispinesib, SB-743921 and GSK-923295, our drug candidates for the treatment of cancer, are currently our only drug candidates in clinical trials and we cannot be



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certain that the clinical development of these or any future drug candidate 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.

***We currently finance and plan to continue to finance our operations through the sale of equity, strategic alliances and debt financings, which may result in additional dilution to our stockholders, relinquishment of valuable technology rights or the imposition of restrictive covenants, or which 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 GSK, Amgen, AstraZeneca and others, equipment financings, interest on investments and government grants. We believe that our existing cash and cash equivalents, future payments from GSK and Amgen, interest earned on investments, proceeds from equipment financings and potential proceeds from our 2007 CEFF 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, strategic alliances or debt financings. 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, such financing may involve covenants that restrict our business activities. In addition, there can be no assurance that any such funding, if needed, will be available on favorable terms, or at all. If we can not raise the funds we need on favorable terms, or at all, our ability to conduct our business will be significantly harmed and our stock price could be negatively affected.

***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 been demonstrated to be safe and effective in clinical trials and there is no assurance that they will. In addition, for each of our current preclinical compounds, we must adequately demonstrate satisfactory chemistry, formulation, stability and toxicity in order to file an investigational new drug application, or IND, 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 significantly harmed and our stock price could 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. 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. For example, although preclinical testing indicated that ispinesib causes tumor regression in a variety of tumor types, to date Phase II clinical trials of ispinesib have not shown clinical activity in a number of different tumor types. Similarly, early-stage clinical trials in healthy volunteers do not necessarily 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 the clinical

trials for any of our drug candidates is focused on appropriate indications, tumor types, patient populations, dosing regimens, safety or efficacy parameters, or other variables which will result in obtaining the desired safety or efficacy data to support regulatory approval to commercialize the drug. For example, in a number of two-stage Phase II clinical trials designed to evaluate the safety and efficacy of ispinesib as monotherapy in the first- or second-line treatment of patients with different forms of cancer, ispinesib did not satisfy the criteria for advancement to Stage 2. Also, there can be no assurance that the methods we select to assess particular safety or efficacy parameters will yield the same statistical precision in their estimation of our drug candidates' effects as

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may other alternative methodologies. 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 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 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. For example, 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, intolerable doses of CK-1827452 were associated with complaints of chest discomfort, palpitations, dizziness and feeling hot, increases in heart rate, declines in blood pressure, electrocardiographic changes consistent with acute myocardial ischemia and transient rises in cardiac troponins I and T, which are markers of possible myocardial injury. If these or other adverse effects are severe or frequent enough to outweigh the potential efficacy of a drug candidate, our clinical trials for such drug candidate may be halted, delayed or interrupted. Furthermore, the FDA or other regulatory authorities could deny approval of such drug candidate 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 significantly harm our reputation and business and negatively affect our stock price.

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

Clinical trials are very expensive and difficult to design and implement, especially in the heart failure and cancer indications that we are pursuing, in part because they are subject to rigorous requirements. The clinical trial process is also time-consuming. In addition, we will need to develop appropriate formulations of our drug candidates for use in clinical trials, such as an oral formulation of CK-1827452. 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, or inability to obtain, regulatory or other approvals to commence and conduct clinical trials in the manner we or our partners deem necessary for the appropriate and timely development of our drug candidates and commercialization of any resulting drugs;

delays in identifying and reaching agreement, or inability to identify and reach agreement, on acceptable terms with prospective clinical trial sites;

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delays or additional costs in developing, or inability to develop, appropriate formulations of our drug candidates for clinical trial use;

slower than expected rates of patient recruitment and enrollment, including as a result of patients', investigators or sites' reluctance to agree to the requirements of a protocol or the introduction of alternative therapies or drugs by others;

for those drug candidates that are the subject of a strategic alliance, delays in reaching agreement with our partner as to appropriate development strategies;

an IRB may require changes to a protocol that then require approval from regulatory agencies and other IRBs, or regulatory authorities may require changes to a protocol that then require approval from the IRBs;

for clinical trials conducted outside of the United States, difficulties in interpreting foreign regulatory requirements or changes in those requirements;

lack of effectiveness during clinical trials;

unforeseen safety issues;

inadequate supply of clinical trial materials;

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, 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 resources that we currently have to carry out such development are limited. Pursuant to our collaboration and option agreement with Amgen, we are responsible for conducting Phase II clinical development for our drug candidate CK-1827452. We cannot engage another strategic partner for CK-1827452 until Amgen elects not to exercise its option to conduct later-stage clinical development for CK-1827452 or its option expires. If Amgen elects not to exercise its option to conduct later-stage clinical development for CK-1827452, we do not have an alternative strategic partner for that drug candidate. Pursuant to our amended collaboration and license agreement with GSK, we are responsible for conducting clinical development for our drug candidates ispinesib and SB-743921. Currently, we rely on GSK to conduct preclinical and clinical

development for GSK-923295 and the NCI to conduct certain clinical trials for ispinesib. We cannot engage another strategic partner for ispinesib or SB-743921 until GSK's option to conduct later-stage clinical development for that drug candidate expires. If GSK elects to terminate its development activities with respect to GSK-923295, or not to exercise its option to conduct later-stage clinical development for either of ispinesib or SB-743921, we do not have an alternative strategic partner for these drug candidates.

For our drug candidates for which we expect to conduct clinical trials at our expense, such as CK-1827452, ispinesib and SB-743921, 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 activities on our own or through the use of other third parties, such as contract research organizations, or CROs, and will incur significant additional costs.

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We utilize CROs for our clinical trials within and outside of the United States. We do not have control over many aspects of our CROs' activities, and cannot fully control the amount or timing of resources that they devote to our programs. CROs 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. Outside of the United States, we are particularly dependent on our CROs' expertise in communicating with clinical trial sites and regulatory authorities and ensuring that our clinical trials and related activities and regulatory filings comply with applicable local laws. The failure of CROs to carry out development activities on our behalf according to our requirements and the FDA's or other regulatory agencies' standards and in accordance with applicable laws, or our failure to properly coordinate and manage such activities, 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 to effectively manage our CROs carrying out such development, or if such CROs fail to perform as agreed, the commercialization of our drug candidates will be delayed or prevented.

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

Under our strategic alliance, GSK is responsible for the clinical development and obtaining and maintaining regulatory approval of our 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, subject to our right to co-promote GSK-923295 in North America if we exercise our option to co-fund certain later-stage development activities for GSK-923295. However, even if we do exercise our option to co-fund the development of GSK-923295, 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. In addition, even if the FDA or other regulatory agencies approve GSK-923295, GSK may elect not to proceed with the commercialization of the resulting drug. 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 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. If GSK abandons development of GSK-923295 prior to regulatory approval or if it elects not to proceed with commercialization of the resulting drug following regulatory approval, we would have to seek a new partner for clinical development or commercialization, curtail or abandon such clinical development or commercialization, or undertake and fund the clinical development of GSK-923295 or commercialization of the resulting drug ourselves. If we seek a new partner but are unable to do so on acceptable terms, or at all, or do not have sufficient funds to conduct such development or commercialization ourselves, we would have to curtail or abandon such development or commercialization, which could harm our business.





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

Our strategy for developing, manufacturing and commercializing certain of our drug candidates and potential 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.

Our collaboration and license agreement with GSK grants it an option relating to development and commercialization rights for either or both of ispinosib and SB-743921. Our collaboration and option agreement with Amgen grants it an option relating to development and commercialization rights for CK-1827452. Each of GSK and Amgen can exercise its option during a defined period by paying us a specified option fee. We may be unable to provide to either or both of GSK and Amgen the necessary data to inform their decisions as to whether to exercise their respective options within our anticipated timeframe, or at all. In addition, either or both of GSK and Amgen may elect not to exercise its option, irrespective of the data that we provide to them. If GSK elects not to exercise its option for either or both of ispinosib and SB-743921, or Amgen elects not to exercise its option for CK-1827452, we do not have alternative strategic partners for these programs. Accordingly, we may have to limit the size or scope of, or delay, one or more of our these programs or undertake and fund these programs ourselves. Similarly, we expect to rely on strategic partners to advance and develop certain compounds from our skeletal muscle contractility and smooth muscle contractility programs. We may not be able to negotiate such strategic alliances on acceptable terms, if at all. If we are not able to establish and maintain such strategic alliances, we may have to limit the size or scope of, or delay, one or more of our these 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 November 2006 amendment to our collaboration and license agreement with GSK through which we assumed responsibility for the clinical development of ispinosib 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 activities depends in part on the performance of our strategic partners 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 ispinosib 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. In addition, if GSK exercises its option with respect to either or both of ispinosib and SB-743921, or if Amgen exercises its option with respect to CK-1827452, they will then be responsible for the clinical development of those respective drug candidates. We have no control over the conduct of clinical development being conducted or that may be conducted in the future by GSK, the NCI or Amgen, including the

timing of initiation, termination or completion of 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.

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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 rely on GSK to be responsible for such activities for the ongoing clinical development of GSK-923295. For CK-1827452, ispinesib, SB-743921 and any future drug candidates for which we conduct clinical development, we rely on a limited number of contract manufacturers, and, in particular, we rely on single-source contract manufacturers for the active pharmaceutical ingredient and the drug product supply for our clinical trials. 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 failure to detect or control anticipated or unanticipated manufacturing errors or the frequent occurrence of such 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. Each contract manufacturer must pass a pre-approval inspection before we can obtain marketing approval for any of our drug candidates and following approval will be subject to 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 pass its pre-approval inspection or maintain ongoing compliance, the production of our drug candidates could be interrupted, resulting in delays, additional costs and potentially lost revenues.

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 economical 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 or cost-effective 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, before a drug from any replacement manufacturer or manufacturing site can be

commercialized, the FDA must approve that site. Such approval would require new testing and compliance inspections. A new manufacturer or manufacturing site also 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

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impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all, which would delay or prevent our ability to commercialize our drugs.

***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 commercialization of 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 or during shipping and storage of the finished product or active pharmaceutical ingredients. 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 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 and Amgen, 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.

With or without a partner, we plan to commercialize on our own drugs 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, cost-effectively 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, our business and reputation will suffer and the price of our common stock could decrease.

***Our focus on the discovery and development 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 and potential drug candidates will appropriately modulate the targeted cytoskeletal proteins and

pathways or produce commercially viable drugs that safely and effectively treat heart failure, cancer 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.

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

Our commercial success will depend in part on our obtaining and maintaining patent and trade secret protection of our technologies, drug candidates and potential drug candidates as well as successfully defending these patents against third-party challenges. We will only be able to protect our technologies, drug candidates and potential 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 CK-1827452, ispinesib, SB-743921 and GSK-923295, 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 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 partners' employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our information to competitors. In addition, confidentiality agreements, if any, executed by such persons may not be enforceable or provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure. If we were to enforce a claim that a third party had illegally obtained and was using our trade secrets, our enforcement efforts would be expensive and time consuming, and the outcome would be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, if our competitors independently develop information that is equivalent to

our trade secrets, it will be more difficult for us to enforce our rights and our business could be harmed.

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



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***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 therapeutic areas in which we are developing drug candidates and exploring for new potential drug candidates. 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.

Patent protection is afforded on a country by country basis. Currently, 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 U.S. patent claims a method of use for inhibiting signaling by what is called the hedgehog pathway using certain such compounds. Curis also 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. One of the European patents which we opposed was recently revoked and is no longer valid in Europe. Curis has appealed this decision. Curis or a third party may assert that the sale of ispienesib may infringe one or more of these 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 any additional oppositions would be successful. We have not attempted to obtain a license to these patents. 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 Bayer AG, Merck, Merck GMBH, Lilly, BMS, Array, ArQule, and AstraZeneca). Further development of these products could be impacted by these patents and result in 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

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.

If any of these events occur, it could significantly harm our business and negatively affect our stock price.

***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

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these inventions. In addition, our research collaborators and scientific advisors have contractual rights to publish 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, could benefit our current or potential competitors and 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 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 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.

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### ***The failure to attract and retain skilled personnel could impair our drug development and commercialization activities.***

Our performance is substantially dependent on the performance of our senior management and key scientific and technical personnel. The loss of the services of any member of our senior management, scientific or technical staff may significantly delay or prevent the achievement of drug development and other business objectives by diverting management's attention to transition matters and identification of suitable replacements, and could have a material adverse effect on our business, operating results and financial condition. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us.

In addition, we believe that we will need to recruit additional executive management and scientific and technical personnel. There is currently intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. Our inability to attract and retain sufficient scientific, technical and managerial personnel could limit or delay our product development activities, 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 cardiovascular diseases, cancer and other diseases for which our compounds may be useful treatments. For example, 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 marketed drugs such as nesiritide, as well as potentially against other novel drug candidates in development such as urocortin II, which is being developed by Neurocrine; ularitide, which is being developed by PDL; CD-NP, which is being developed by Nile; and levosimendan, which is being developed in the United States by Abbott, in collaboration with Orion, and is commercially available in a number of countries outside of the United States.

Similarly, if approved for marketing by the FDA, depending on the approved clinical indication, our anti-cancer drug candidates such as ispinesib, SB-743921 and GSK-923295 could compete against existing cancer treatments such as paclitaxel, docetaxel, vincristine, vinorelbine, navelbine, ixabepilone and potentially against other novel anti-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, AstraZeneca, Kosan, Roche and other pharmaceutical and biopharmaceutical companies are developing other approaches to inhibiting mitosis.

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;

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

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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 NDA approval 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, 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 fail to receive and maintain regulatory approval for the sale of any drugs resulting from our drug candidates, it would significantly harm our business and negatively affect our stock price.



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***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 would 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

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

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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 or other 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. Our insurance does not cover third parties' negligence or malpractice, and our clinical investigators and sites may have inadequate insurance or none at all. In addition, in order to conduct clinical trials or otherwise carry out our business, we may have to contractually assume liabilities for which we may not be insured. If we are unable to look to our own or a third party's insurance to pay claims against us, we may have to pay any arising costs and damages ourselves, which may be substantial.

In addition, once we have commercially launched drugs based on our drug candidates, we will face even greater 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 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 significantly harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and distract management.

***We use hazardous chemicals and radioactive and biological materials in our business. Responding to 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 activities.

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

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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, which could be costly and time-consuming and distract management.

***Our facilities in California are located near an earthquake fault, and an earthquake or other types of natural disasters, catastrophic events or resource shortages could disrupt our operations and adversely affect our 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, a catastrophic event such as a disease pandemic or terrorist attack 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. Our partners and other third parties on which we rely may also be subject to business interruptions from such events. 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**

***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 heart failure or cancer, including the current and proposed clinical trials for CK-1827452 for heart failure, ispinesib for leukemia, pediatric solid tumors and breast cancer, SB-743921 for Hodgkin and non-Hodgkin lymphoma, and GSK-923295 for cancer, and including delays resulting from slower than expected or suspended patient enrollment or discontinuations resulting from a failure to meet pre-defined clinical end-points;

announcements concerning our strategic alliances with Amgen, 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;

developments in establishing new strategic alliances;

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;

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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 February 29, 2008, our executive officers, directors and their affiliates beneficially owned or controlled approximately 26% 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.

***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, or Sarbanes-Oxley, new Securities and Exchange Commission regulations and NASDAQ Stock Market LLC 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, 2007, 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, which could be costly and time-consuming, 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 The NASDAQ Global Market, or 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



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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, and could harm our reputation and business.

***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.

## **Risks Related To Our Financing Vehicles and Investments**

***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 2007, we entered into the 2007 CEFF with Kingsbridge. The 2007 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 2007 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 the registration statement registering for resale the shares of common stock to be issued in connection with the 2007 CEFF; and the continued listing of our stock on NASDAQ. In addition, Kingsbridge is permitted to terminate the 2007 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 2007 CEFF, or if the 2007 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 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 registration statement, the blackout or other payment could be significant.

Should we sell shares to Kingsbridge under the 2007 CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effect 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 2007 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 2007 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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***If the recent worsening of credit market conditions continues or increases, it could have an adverse impact on our investment portfolio or our operations.***

Recent U.S. sub-prime mortgage defaults have had a significant impact across various sectors of the financial markets, causing global credit and liquidity issues. The short-term funding markets experienced credit issues during the second half of fiscal year 2007 and early fiscal year 2008 leading to liquidity disruption in asset-backed commercial paper and failed auctions in the auction rate market. To date, we have not recorded an impairment charge related to our auction rate securities that we hold in our investment portfolio. However, if the global credit market continues to deteriorate, our investment portfolio may be adversely impacted and we could determine our investments are impaired. This could adversely impact our results of operations and financial condition. Furthermore, in light of auction failures associated with our auction rate securities, we re-classified our auction rate securities as long term investments due to the uncertainty associated with the timing of our ability to access the funds underlying these investments. If we are unable to access the funds underlying these investments in a timely manner, we may need to find alternate sources of funding for certain of our operations, which may not be available on favorable terms, or at all, and our business could be adversely effected.

**Item 1B. *Unresolved Staff Comments***

There are no unresolved staff comments regarding any of our periodic or current reports.

**Item 2. *Properties***

Our facilities consist of approximately 81,587 square feet of research and office space. We lease 50,195 square feet located at 280 East Grand Avenue in South San Francisco, California until 2013 with an option to renew that lease over that timeframe. We also lease 31,392 square feet at 256 East Grand Avenue in South San Francisco, California until 2011. We believe that these facilities are suitable and adequate for our current needs.

**Item 3. *Legal Proceedings***

We are not a party to any material legal proceedings.

**Item 4. *Submission of Matters to a Vote of Security Holders***

There were no matters submitted to a vote of the security holders during the fourth quarter of 2007.

Table of Contents**PART II****Item 5. *Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Our common stock is quoted on the NASDAQ Global Market under the symbol CYTK, and has been quoted on such market since our initial public offering on April 29, 2004. Prior to such date, there was no public market for our common stock. The following table sets forth the high and low closing sales price per share of our common stock as reported on the NASDAQ Global Market for the periods indicated.

|                     | <b>Closing Sale Price</b> |            |
|---------------------|---------------------------|------------|
|                     | <b>High</b>               | <b>Low</b> |
| <b>Fiscal 2006:</b> |                           |            |
| First Quarter       | \$ 7.95                   | \$ 6.18    |
| Second Quarter      | \$ 7.94                   | \$ 6.26    |
| Third Quarter       | \$ 7.20                   | \$ 5.32    |
| Fourth Quarter      | \$ 7.99                   | \$ 6.21    |
| <b>Fiscal 2007:</b> |                           |            |
| First Quarter       | \$ 8.60                   | \$ 6.56    |
| Second Quarter      | \$ 7.38                   | \$ 5.65    |
| Third Quarter       | \$ 5.77                   | \$ 4.58    |
| Fourth Quarter      | \$ 6.25                   | \$ 4.40    |

On February 29, 2008, the last reported sale price for our common stock on the NASDAQ Global Market was \$3.37 per share. We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and have not paid and do not in the foreseeable future anticipate paying any cash dividends. As of February 29, 2008, there were 148 holders of record of our common stock.

On December 29, 2006, in connection with entering into a collaboration and option agreement with Amgen, we contemporaneously entered into a common stock purchase agreement with Amgen, which provided for the sale of 3,484,806 shares of our common stock at a price per share of \$9.47, an aggregate purchase price of approximately \$33.0 million, and a Registration Rights Agreement that provides Amgen with certain registration rights with respect to these shares. The shares were issued to Amgen on January 2, 2007. Pursuant to the terms of the common stock purchase agreement, Amgen has agreed to certain trading and other restrictions with respect to our common stock. We relied on the exemption from registration contained in Section 4(2) of the Securities Act in connection with the issuance and sale of the shares to Amgen.

There were no employee stock repurchases for the quarter ended December 31, 2007. As of December 31, 2007, there were no remaining shares of common stock subject to repurchase by us.

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**Equity Compensation Information**

Information regarding our equity compensation plans and the securities authorized for issuance thereunder is set forth in Part III, Item 12.

**Comparison of Historical Cumulative Total Return (\*) Among Cytokinetics, Incorporated, the NASDAQ Stock Market (U.S.) Index and the NASDAQ Biotechnology Index**

(\*) The above graph shows the cumulative total stockholder return of an investment of \$100 in cash on April 29, 2004, the date our common stock began to trade on the NASDAQ Global Market, through December 31, 2007 for: (i) our common stock; (ii) the NASDAQ Stock Market (U.S.) Index; and (iii) the NASDAQ Biotechnology Index. All values assume reinvestment of the full amount of all dividends. Stockholder returns over the indicated period should not be considered indicative of future stockholder returns.

|                                  | <b>4/29/04</b> | <b>12/31/07</b> |
|----------------------------------|----------------|-----------------|
| Cytokinetics, Incorporated       | \$ 100.00      | \$ 29.09        |
| NASDAQ Stock Market (U.S.) Index | \$ 100.00      | \$ 138.13       |
| NASDAQ Biotechnology Index       | \$ 100.00      | \$ 106.81       |

The information contained under this caption Comparison of Historical Cumulative Total Return(\*) Among Cytokinetics, Incorporated, the NASDAQ Stock Market (U.S.) Index and the NASDAQ Biotechnology Index shall not be deemed to be soliciting material or to be filed with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the we specifically incorporate it by reference into such filing.

**Table of Contents****Item 6. Selected Financial Data**

The following selected financial data should be read in conjunction with Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations and Item 8, Financial Statements and Supplemental Data of this Form 10-K.

|   | <b>Year Ended December 31,</b>                  |             |             |             |             |
|---|---|-------------|-------------|-------------|-------------|
|   | <b>2007</b>                                     | <b>2006</b> | <b>2005</b> | <b>2004</b> | <b>2003</b> |
|   | <b>(In thousands, except per share amounts)</b> |             |             |             |             |
| <b>Statement of Operations Data:</b>  |   |             |             |             |             |
| Revenues:   |   |             |             |             |             |
| Research and development revenues from related party  | \$ 1,388  | \$ 1,622    | \$ 4,978    | \$ 9,338    | \$ 7,692    |
| Research and development, grant and other revenues  |   | 4           | 1,134       | 1,304       | 85          |
| License revenues from related parties   | 12,234  | 1,501       | 2,800       | 2,800       | 2,800       |
| Total revenues  | 13,622  | 3,127       | 8,912       | 13,442      | 10,577      |
| Operating expenses:   |   |             |             |             |             |
| Research and development  | 53,388  | 49,225      | 40,570      | 39,885      | 34,195      |
| General and administrative  | 16,721  | 15,240      | 12,975      | 11,991      | 8,972       |
| Total operating expenses  | 70,109  | 64,465      | 53,545      | 51,876      | 43,167      |
| Operating loss  | (56,487)  | (61,338)    | (44,633)    | (38,434)    | (32,590)    |
| Interest and other income   | 8,292   | 4,746       | 2,916       | 1,785       | 903         |
| Interest and other expense  | (699)   | (523)       | (535)       | (549)       | (998)       |
| Net loss  | \$ (48,894)                                     | \$ (57,115) | \$ (42,252) | \$ (37,198) | \$ (32,685) |
| Net loss per common share - basic and diluted(2)  | \$ (1.03)                                       | \$ (1.56)   | \$ (1.48)   | \$ (1.88)   | \$ (17.09)  |
| Weighted average shares used in computing net loss per common share basic and diluted(1)(2) | 47,590  | 36,618      | 28,582      | 19,779      | 1,912       |

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|  | <b>As of December 31,</b> |             |             |             |             |
|--|---------------------------|-------------|-------------|-------------|-------------|
|  | <b>2007</b>               | <b>2006</b> | <b>2005</b> | <b>2004</b> | <b>2003</b> |
|  | <b>(In thousands)</b>     |             |             |             |             |
| <b>Balance Sheet Data:</b>                                     |                           |             |             |             |             |
| Cash, cash equivalents and short- and long-term investments(1) | \$ 139,764                | \$ 109,542  | \$ 76,212   | \$ 110,253  | \$ 42,332   |
| Restricted cash  | 5,167                     | 6,034       | 5,172       | 5,980       | 7,199       |
| Working capital  | 95,568                    | 127,228     | 67,600      | 98,028      | 27,619      |
| Total assets   | 155,370                   | 169,516     | 91,461      | 128,101     | 62,873      |
| Long-term portion of equipment financing lines                 | 4,639                     | 7,144       | 6,636       | 8,106       | 8,075       |
| Deficit accumulated during the development stage               | (279,533)                 | (230,639)   | (173,524)   | (131,272)   | (94,074)    |
| Total stockholders equity (deficit)(1)                         | 155,370                   | 106,313     | 73,561      | 107,556     | (92,031)    |

- (1) Our initial public offering was declared effective by the Securities and Exchange Commission on April 29, 2004 and our common stock commenced trading on that date. We sold 7,935,000 shares of common stock in the offering for net proceeds of approximately \$94.0 million. In addition, we sold 538,461 shares of our common stock to GSK immediately prior to the closing of the initial public offering for net proceeds of approximately \$7.0 million. Also in conjunction with the initial public offering, all of the outstanding shares of our convertible preferred stock were converted into 17,062,145 shares of our common stock. In December 2005, we sold 887,576 shares of common stock to Kingsbridge pursuant to the CEFF we entered into with Kingsbridge in 2005 for net proceeds of \$5.5 million. In 2006, we sold 10,285,715 shares in two registered direct offerings for net proceeds of approximately \$66.9 million, and sold 2,740,735 shares of common stock to Kingsbridge pursuant to the 2005 CEFF for net proceeds of \$17.0. In 2007, we sold 2,075,177 shares of common stock to Kingsbridge pursuant to the 2005 CEFF for net proceeds of \$9.5 million. In January 2007, we issued 3,484,806 shares of Company common stock to Amgen for net proceeds of \$32.9 million in connection with a common stock purchase agreement with Amgen.
- (2) All share and per share amounts have been retroactively adjusted to give effect to the 1-for-2 reverse stock split that occurred on April 26, 2004.

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

This discussion and analysis should be read in conjunction with our financial statements and accompanying notes included elsewhere in this report. Operating results are not necessarily indicative of results that may occur in future periods.

**Overview**

We are a biopharmaceutical company, incorporated in Delaware in 1997, focused on developing small molecule therapeutics for the treatment of cardiovascular diseases and cancer. Our current development activities are primarily directed to advancing multiple drug candidates through clinical trials with the objective of determining the intended pharmacodynamic effect or effects in two principal diseases: heart failure and cancer. Our drug development pipeline consists of a drug candidate, CK-1827452, being developed in both an intravenous and oral formulation for the potential treatment of heart failure, and three drug candidates, ispinesib, SB-743921 and GSK-923295, each being

developed in an intravenous formulation for the potential treatment of cancer. Our drug candidates are all novel small molecules that arose from our research activities and are directed toward the biology of the cytoskeleton. We believe our understanding of the cytoskeleton enables us to discover novel and potentially safer and more effective therapeutics.

***Cardiovascular Program:***

Our drug candidate, CK-1827452, a novel cardiac myosin activator for the potential treatment of heart failure, is currently being developed as part of a clinical trials program, comprised of Phase I and Phase IIa



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trials, designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of this drug candidate in both an intravenous and oral formulation.

In April 2007, we initiated a Phase IIa, multi-center, double-blind, randomized, placebo-controlled, dose-escalation clinical trial of CK-1827452 in patients with stable heart failure. The primary objective of this trial is to evaluate the safety and tolerability of CK-1827452 administered as an intravenous infusion to stable heart failure patients. The secondary objectives of this trial are to establish a relationship between plasma concentration and pharmacodynamic effects of CK-1827452 and to determine the pharmacokinetics of CK-1827452 in stable heart failure patients.

In April 2007, we initiated a single-center, open-label, sequential, parallel group, Phase I clinical trial designed to evaluate potential drug-drug interactions with CK-1827452. The trial is designed to evaluate the effects of oral ketoconazole, a strong metabolic inhibitor of P450 (CYP) 3A4, and diltiazem, a moderate CYP3A4 inhibitor, on the pharmacokinetics of CK-1827452 given in an intravenous formulation to healthy volunteers.

In July 2007, we initiated a single-center, two-part, open label, Phase I clinical trial of CK-1827452 designed to evaluate the pharmacokinetics and relative bioavailability of three different oral modified release prototypes.

***Oncology Program:***

Ispinesib, our most advanced drug candidate, has been the subject of a broad Phase II clinical trials program under the sponsorship of GlaxoSmithKline, or GSK, and the National Cancer Institute, or NCI, designed to evaluate its efficacy against multiple tumor types. We have reported Phase II clinical trials data from this program in metastatic breast, non-small cell lung, ovarian, colorectal, head and neck, hepatocellular, renal and prostate cancers and in melanoma. To date, we believe clinical activity for ispinesib has been observed in non-small cell lung cancer, ovarian and breast cancers, with the most robust clinical activity observed in a Phase II clinical trial evaluating ispinesib in the treatment of patients with locally advanced or metastatic breast cancer that had failed treatment with taxanes and anthracyclines. We are conducting, at our expense, a focused development program for ispinesib in the treatment of patients with locally advanced or metastatic breast cancer. This program is intended to build upon the previous data from the clinical trials conducted by GSK and the NCI, and is designed to further define the clinical activity profile of ispinesib in advanced breast cancer patients in preparation for potentially initiating a Phase III clinical trial of ispinesib for the second-line treatment of advanced breast cancer. In December 2007, we initiated a Phase I/II monotherapy clinical trial designed to evaluate ispinesib in the first-line treatment of chemotherapy-naïve patients with locally advanced or metastatic breast cancer on a more dose-dense schedule than was previously studied.

We continue to enroll and dose-escalate patients in an open-label, non-randomized Phase I/II clinical trial of SB-743921, our second drug candidate for the treatment of cancer, in order to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile in patients with Hodgkin or non-Hodgkin lymphoma. In December 2007, interim data from this ongoing trial was presented at the Annual Meeting of the American Society of Hematology.

In August 2007, we announced that GSK had initiated a first-time-in-humans Phase I clinical trial of GSK-923295. This clinical trial is an open-label, non-randomized, dose-finding trial designed to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of GSK-923295 in patients with advanced solid tumors. The initiation of this clinical trial triggered a milestone payment of \$1.0 million from GSK to Cytokinetics under our collaboration and license agreement with GSK, or GSK Agreement.

Ispinesib, SB-743921 and GSK-923295 are being developed in connection with our strategic alliance with GSK, established in 2001, which is focused on novel small molecule therapeutics targeting human mitotic kinesins for applications in the treatment of cancer and other diseases. Pursuant to our November 2006 amendment to the GSK Agreement, we have assumed responsibility for the continued development of ispinesib and SB-743921, at our expense, and subject to GSK's option to resume responsibility for some or all development and commercialization activities associated with either or both of these novel drug candidate, exercisable during a defined period. If GSK does not exercise its option for either ispinesib or SB-743921, we will be obligated to pay royalties to GSK on the sales of any resulting products. The November 2006 amendment supersedes a previous amendment to the

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collaboration agreement dated September 2005, which specifically related to SB-743921. Cytokinetics and GSK continue to conduct collaborative research activities directed to inhibitors of centromere-associated protein E, or CENP-E, including GSK-923295, pursuant to a June 2006 amendment to the strategic alliance.

We are also pursuing other early research programs addressing a number of therapeutic areas, including the potential treatment of hypertension, asthma and neuromuscular diseases.

Since our inception in August 1997, we have incurred significant net losses. As of December 31, 2007, we had an accumulated deficit of \$279.5 million. We expect to incur substantial and increasing losses for the next several years if and to the extent:

- we advance CK-1827452 through clinical development for the treatment of heart failure and Amgen does not exercise its option to participate in later-stage development and commercialization;

- we conduct continued Phase I, Phase II and later-stage development and commercialization of ispinesib, SB-743921 or GSK-923295 under our collaboration and license agreement with GSK, as amended;

- we exercise our option to co-fund the development of GSK-923295 or of any other drug candidate being developed by GSK under our strategic alliance;

- we exercise our option to co-promote any of the products for which we have elected co-fund development under our strategic alliance with GSK;

- we advance other potential drug candidates into clinical trials;

- we expand our research programs and further develop our proprietary drug discovery technologies; or

- we elect to fund development or commercialization of any drug candidate.

We intend to pursue selective strategic alliances to enable us to maintain financial and operational flexibility.

## **Cardiovascular**

We have focused our cardiovascular research and development activities on heart failure, a disease most often characterized by compromised contractile function of the heart that impacts its ability to effectively pump blood throughout the body. We have discovered and optimized small molecules that have the potential to improve cardiac contractility by specifically binding to and activating cardiac myosin, a cytoskeletal protein essential for cardiac muscle contraction. This work gave rise to our drug candidate CK-1827452, a novel small molecule cardiac myosin activator. CK-1827452 entered clinical trials in 2006. Based on data from our first-time-in-humans Phase I clinical trial with this drug candidate, in April 2007, we initiated a clinical trials program for CK-1827452, comprised of Phase I and Phase IIa designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of both intravenous and oral formulations of this drug candidate in a diversity of patients, including patients with stable heart failure and patients with ischemic cardiomyopathy. Our goal is to develop CK-1827452 as a potential treatment across the continuum of care in heart failure, both in the hospital setting as an intravenous formulation for the treatment of acutely decompensated heart failure and in the outpatient setting as an oral formulation for the treatment of chronic heart failure. In December 2006, we entered into a collaboration and option agreement with Amgen to discover, develop and commercialize novel small-molecule therapeutics that activate cardiac muscle contractility for potential applications in the treatment of heart failure, including CK-1827452. The agreement provides Amgen with a non-exclusive license and access to certain technology, as well as an exclusive option to participate in future

development and commercialization of CK-1827452 world-wide, excluding Japan. Amgen's option is exercisable during a defined period, the ending of which is dependent upon the satisfaction of certain conditions, primarily the delivery of Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed development plan, the results of which may be sufficient to support its progression into Phase IIb clinical development.

**CK-1827452 (intravenous)**

*Phase I first-time-in-humans:* In 2005, we initiated a first-time-in-humans Phase I clinical trial with CK-1827452. This clinical trial was designed as a double-blind, randomized, placebo-controlled, dose-escalation trial to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of a six-hour infusion of CK-1827452 in healthy volunteers. Clinical data from this trial were presented at the Heart Failure Society of America, or HFSA, meeting in September 2006. The maximum tolerated dose, or MTD, was 0.5 mg/kg/hr for this

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regimen. At this dose, the six-hour infusion of CK-1827452 produced statistically significant mean increases in left ventricular ejection fraction and fractional shortening of 6.8 and 9.2 absolute percentage points, respectively, as compared to placebo. These increases in indices of left ventricular function were associated with a mean prolongation of systolic ejection time of 84 milliseconds, which was also statistically significant. These mean changes in ejection fraction, fractional shortening and ejection time were concentration-dependent and CK-1827452 exhibited generally linear, dose-proportional pharmacokinetics across the range of doses studied. At the MTD, CK-1827452 was well-tolerated when compared to placebo. The adverse effects at the dose levels exceeding the MTD in humans appeared similar to the adverse findings observed in the preclinical safety studies, and occurred at similar plasma concentrations. These effects are believed to be related to an excess of the intended pharmacologic effect, resulting in excessive prolongation of the systolic ejection time, and resolved promptly with discontinuation of the infusions of CK-1827452. The Phase I clinical trial activity of CK-1827452 is consistent with results from preclinical models that evaluated CK-1827452 in normal dogs; however, further clinical trials are necessary to determine whether similar results will also be seen in patients with heart failure. A poster presented at the September 2007 HFSA meeting provided additional data and analysis regarding this trial. The objective of this analysis was to evaluate the concentration-response relationship of CK-1827452 on left ventricular function in healthy volunteers. The authors concluded that CK-1827452 increased left ventricular ejection fraction and left ventricular fractional shortening over a range of well-tolerated plasma concentrations. In addition, it was determined that systolic ejection time was the most sensitive marker of drug effect and that increases in left ventricular ejection fraction and left ventricular fractional shortening were well-correlated with increases in systolic ejection time. Systolic ejection time is easily measured and we believe may serve as a useful indicator of this drug candidate's effect in patients with heart failure.

*Phase IIa stable heart failure:* In April 2007, we initiated a Phase IIa, multiple-center, double-blind, randomized, placebo-controlled, dose-escalation clinical trial of CK-1827452 in patients with stable heart failure. In addition to the trial's primary objective of evaluating the safety and tolerability of CK-1827452, its secondary objectives are to establish a relationship between the plasma concentration and the pharmacodynamic effects of CK-1827452 and to determine its pharmacokinetics in stable heart failure patients. In addition to routine assessments of vital signs, blood samples and electrocardiographic monitoring, echocardiograms will be performed to evaluate cardiac function at various pre-defined time points. The clinical trial will consist of up to five cohorts of eight patients with stable heart failure. The first three of these cohorts will each undergo four treatment periods; patients will receive three escalating active doses of CK-1827452 administered intravenously and one placebo treatment which will be randomized into the dose escalation sequence. Patients in the fourth and fifth cohorts may receive only a single dose level of CK-1827452. In each cohort, patients will receive a one-hour loading infusion to rapidly achieve a target plasma concentration of CK-1827452, followed by a slower infusion intended to maintain that plasma concentration. These maintenance infusions are planned to be one hour in duration in the first two cohorts, and 23 hours in duration in the third cohorts. We have completed the treatment phase for the second cohort of patients in this clinical trial. We anticipate interim data to be available from this trial in the first half of 2008. We anticipate final data to be available from this trial during the second half of 2008.

**CK-1827452 (oral)**

*Phase I oral bioavailability:* In December 2006, we announced results from a Phase I oral bioavailability study of CK-1827452 in healthy volunteers. We believe that these data support our current activities to develop a modified release oral formulation of CK-1827452 to enable late-stage clinical development of a dosing schedule that may be suitable for the treatment of patients with chronic heart failure. This study was designed as an open-label, four-way crossover study in ten healthy volunteers designed to investigate the absolute bioavailability of two oral formulations (liquid and immediate-release solid formulations) of CK-1827452 versus an intravenous dose. In addition, the effect of taking the immediate-release solid formulation in a fed versus fasted state on the relative bioavailability of CK-1827452 was also assessed. Volunteers were administered, in random order, CK-1827452 at 0.125mg/kg as a liquid solution taken orally in a fasted state, an immediate-release solid formulation taken in fed and fasted states and

a reference intravenous infusion at a constant rate over one hour. Pharmacokinetic data from this study demonstrated oral bioavailability of approximately 100% for each of the three conditions of oral administration. The median time to maximum plasma concentrations after dosing was 0.5 hours for the liquid solution taken orally, one hour for the immediate-release solid formulation taken in a fasted state, and 3 hours for the immediate-release solid formulation taken after eating. This rapid and essentially complete oral absorption suggests

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that predictable plasma levels can be achieved with chronic oral dosing in patients with heart failure. A poster summarizing the results of this study was presented at the September 2007 HFSA meeting. The authors concluded that the near complete absolute bioavailability of CK-1827452 suggested that there is little or no first-pass metabolism of this drug candidate. In addition, food did not have a substantial effect on bioavailability but appeared to delay drug absorption in some subjects. CK-1827452, in both the oral and intravenous formulations, was well-tolerated with no significant safety issues observed. The near complete absolute bioavailability suggested that there is little or no first-pass metabolism of this drug candidate. We believe that these data support our current activities to develop a modified release oral formulation of CK-1827452 to enable late-stage clinical development of a dosing schedule that may be suitable for the treatment of patients with chronic heart failure.

*Phase I drug-drug interaction:* In April 2007, we announced the initiation of a single-center, open-label, sequential, parallel group, Phase I clinical trial of CK-1827452 designed to evaluate the effects of oral ketoconazole, a strong inhibitor of the metabolic enzyme cytochrome P450 (CYP) 3A4, on the pharmacokinetics of CK-1827452 given orally to up to 16 healthy male volunteers, 8 of whom have a normal genotype for CYP2D6, and up to eight of whom have reduced CYP2D6 activity. In addition, the effects of diltiazem, a moderate CYP3A4 inhibitor, on the pharmacokinetics of CK-1827452 will be assessed in eight additional volunteers who are normal metabolizers by way of CYP2D6. We continue to enroll subjects with reduced CYP2D6 activity into this trial. We anticipate data from this trial to be available in 2008.

*Phase I multi-dose:* In July 2007, we announced the initiation of a single-center, Phase I clinical trial designed to evaluate the pharmacokinetics of an oral formulation of CK-1827452 in healthy volunteers. The trial progressed from a single-blind, single-dose phase to a randomized, double-blind, placebo-controlled, multi-dose phase. We completed treatment in this trial in December 2007. We anticipate data from this trial to be available in 2008.

*Phase I modified release:* In December 2007, we initiated a single-center, two-part, open-label, Phase I clinical trial of up to twelve healthy male volunteers. The primary objective of this trial is to assess the pharmacokinetics and relative bioavailability of three different oral modified release prototypes of CK-1827452. The secondary objective of the trial is to determine whether there is an effect of food on the pharmacokinetics of one of these oral modified release prototypes of CK-1827452. We anticipate data from this trial to be available in 2008.

***2008 Planned Clinical Trials.***

In the first half of 2008, we anticipate initiating two additional Phase IIa clinical trials of CK-1827452. The first of these clinical trials is intended to evaluate an intravenous form of CK-1827452 in stable heart failure patients undergoing cardiac catheterization. The second is intended to evaluate an intravenous form together with an oral formulation of CK-1827452 in patients with ischemic cardiomyopathy.

CK-1827452 is at too early a stage of development for us to predict if or when we will be in a position to generate any revenues or material net cash flows from its commercialization. We currently fund all research and development costs associated with this program. We recorded research and development expenses for activities relating to our cardiovascular program of approximately \$22.4 million, \$18.1 million and \$19.6 million in the years ended December 31, 2007, 2006 and 2005, respectively. We anticipate that our expenditures relating to the research and development of compounds in our cardiovascular program will increase significantly as we advance CK-1827452 through clinical development. Our expenditures will also increase if Amgen does not exercise its option and we elect to develop CK-1827452 or related compounds independently, or if we elect to co-fund later-stage development of CK-1827452 or other compounds in our cardiovascular program under our collaboration and option agreement with Amgen following Amgen's exercise of its option. If Amgen elects to exercise its option, they would be responsible for development and commercialization of CK-1827452 and related compounds, subject to our development and commercial participation rights. In addition, we may be eligible to receive pre-commercialization and

commercialization milestone payments of up to \$600 million on CK-1827452 and other products arising from the research under the collaboration as well as escalating royalties based on increasing levels of annual net sales of products commercialized under the agreement. The agreement also provides for us to receive increased royalties by co-funding Phase III development costs of drug candidates under the collaboration. If we elect to co-fund such costs, we would be entitled to co-promote products in North America and participate in agreed commercial activities in institutional care settings, at Amgen's expense. If Amgen elects not to exercise its option on



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CK-1827452, we may then independently proceed to develop CK-1827452 and the research collaboration would terminate.

## **Oncology**

In 2007, we continued to advance our oncology development programs for ispinesib and SB-743921 as they progressed in Phase I of their respective Phase I/II clinical trials. In 2006, we entered into two amendments to our collaboration and license agreement with GSK, or the GSK Agreement, regarding the future research, development and commercialization of ispinesib, SB-743921 and CENP-E. In June 2006, we amended the agreement to extend the initial five-year research term of this strategic alliance for an additional year to continue activities focused towards translational research directed to CENP-E. In November 2006, we further amended the agreement and assumed, at our expense, responsibility for the continued research, development and commercialization of inhibitors of kinesin spindle protein, or KSP, including ispinesib and SB-743921, and other mitotic kinesins, other than CENP-E. In June 2007, the agreement was further amended to extend the research term for an additional year, through June 19, 2008, to facilitate continued research activities under the updated research plan focused towards CENP-E. We are also researching other compounds for the potential treatment of cancer.

## **Ispinesib**

The clinical trials program for ispinesib has consisted to date of nine Phase II clinical trials and eight Phase I or Ib clinical trials evaluating the use of this drug candidate in a variety of both solid and hematologic cancers. We believe that the breadth of this clinical trials program has taken into consideration the potential and the complexity of developing a drug candidate such as ispinesib, and should help us to identify those tumor types and dosing regimens that are the most promising for the continued development of ispinesib. We have reported Phase II clinical trial data for ispinesib in metastatic breast, non-small cell lung, ovarian, colorectal, head and neck, hepatocellular, renal and prostate cancers and in melanoma. To date, we believe clinical activity for ispinesib has been observed in non-small cell lung cancer, ovarian and breast cancer, with the most robust clinical activity observed in a Phase II clinical trial evaluating ispinesib in the treatment of patients with locally advanced or metastatic breast cancer that had failed treatment with taxanes and anthracyclines. Under our strategic alliance with GSK, we have initiated a focused development program for ispinesib in the treatment of patients with locally advanced or metastatic breast cancer. This program is intended to build upon the previous data from the clinical trials conducted by GSK and the NCI, and is designed to further define the clinical activity profile of ispinesib in chemotherapy-naïve locally advanced or metastatic breast cancer patients in preparation for potentially initiating a later stage clinical trials program of ispinesib for the second-line treatment of advanced breast cancer.

Currently ongoing and recently completed clinical trials of ispinesib are as follows:

*Breast Cancer:* In June 2007, we announced the final results from a multicenter Phase II clinical trial sponsored by GSK, which evaluated the safety and efficacy of ispinesib in the second- or third-line treatment of patients with locally advanced (Stage IIIB) or metastatic (Stage IV) breast cancer whose disease had recurred or progressed despite treatment with anthracyclines and taxanes. In this trial, patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The primary endpoint of the clinical trial was objective response as determined using the Response Evaluation Criteria in Solid Tumors, or RECIST. The best overall responses observed with ispinesib were partial responses in 4 of 45 evaluable patients as measured by RECIST and the duration of response ranged from 7.1 weeks to 30.0 weeks. The most common adverse event was Grade 4 neutropenia.

Based on these data, and consistent with our focused approach to the further development of ispinesib, in December 2007, we initiated an open-label, non-randomized Phase I/II clinical trial designed to evaluate ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast

cancer. This trial is designed to be a proof-of-concept study to potentially amplify the signals of clinical activity seen in GSK's Phase II monotherapy trial of ispinesib in breast cancer, and is intended to provide the data necessary to inform ispinesib's further development, as well as to inform GSK's potential exercise of its option to develop and commercialize ispinesib. The Phase I portion of the Phase I/II trial is designed to determine the dose-limiting toxicity and MTD of ispinesib as monotherapy administered as a one-hour intravenous infusion on days 1 and 15 of a 28-day cycle in female patients with locally advanced or metastatic adenocarcinoma of the breast who have not received prior chemotherapy. Once an MTD is determined, the clinical trial is planned to move into Phase II, which

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is designed to assess the overall response rate of ispinesib in patients with measurable locally advanced or metastatic breast cancer who have not received prior chemotherapy, using RECIST. In the Phase II portion of this clinical trial, ispinesib is planned to be administered as a one-hour intravenous infusion on days 1 and 15 of a 28-day treatment cycle at the MTD determined in Phase I.

*Ovarian Cancer:* In June 2007 at the Annual Meeting of the American Society of Clinical Oncology, or ASCO, GSK presented data from Stage 1 of a two-stage Phase II trial of ispinesib as monotherapy in patients with platinum/taxane refractory or resistant relapsed ovarian cancer. The primary objective of this clinical trial was to evaluate the overall response rate with secondary objectives measuring the median time to radiographic response, median time to CA-125 response, median duration of radiographic response and progression-free survival. The best radiographic response was 1 partial response with a duration of 42 weeks and 5 patients with stable disease. Although a radiographic response was observed, none of the 22 evaluable patients had a CA-125 response and the median time to CA-125 progression was 5.3 weeks. In this clinical trial, the protocol-specific criteria to proceed to Stage 2 were not met. The most common adverse event was Grade 4 neutropenia.

*Renal Cell Cancer:* Included in the June 2007 ASCO proceedings was an abstract which presented interim data from a two-stage Phase II clinical trial of ispinesib in patients with advanced renal cell carcinoma sponsored by the NCI. The primary objective of this clinical trial was to assess overall response rate using RECIST. Secondary objectives included evaluating toxicities, time to progression and overall survival. In this clinical trial, 19 patients were enrolled and received ispinesib as monotherapy at 7 mg/m<sup>2</sup> as a one-hour infusion on days 1, 8 and 15 every 28 days with radiologic disease re-evaluation every 8 weeks. Of the 15 evaluable patients included in the interim analysis, the best response observed was stable disease in 7 patients after 8 weeks. One patient experienced Grade 3 neutropenia but no other Grade 3 or 4 toxicities were deemed to be attributable to the study drug. The authors concluded that treatment with ispinesib as a monotherapy at this dose and schedule in this patient population does not appear to lead to objective responses but appears to be well-tolerated.

*Prostate Cancer:* In June 2007, we announced results from Stage 1 of the NCI's two-stage, Phase II clinical trial for the treatment of patients with hormone refractory prostate cancer who had failed taxane-based chemotherapy, in which 21 patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. No patients met the primary endpoint of objective response as determined by blood levels of the tumor mass marker Prostate Specific Antigen or PSA and the median time to PSA or clinical progression was 9 weeks. Ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The most common adverse event was Grade 4 neutropenia.

*Hepatocellular Cancer:* In June 2007, we announced the results from Stage 1 of the NCI's two-stage, Phase II clinical trial for the treatment of hepatocellular cancer, in which 15 patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The best overall response was stable disease seen in 7 of the 15 patients. Ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The most common adverse event was Grade 4 neutropenia.

*Melanoma:* In June 2007, we announced the results from Stage 1 of the NCI's two-stage, Phase II clinical trial for the treatment of patients with chemotherapy-naïve recurrent or metastatic malignant melanoma, in which 17 patients received ispinesib as monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The best overall response was stable disease seen in 6 of 17 patients treated. Ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The most frequent Grade 3 or 4 hematologic adverse events were neutropenia and lymphopenia.

*Ispinesib with capecitabine:* In the second quarter of 2007, GSK concluded patient treatment in a dose-escalating, Phase Ib clinical trial evaluating the safety, tolerability and pharmacokinetic profile of ispinesib in combination with

capecitabine. In 2006, interim clinical trial data were presented demonstrating that the combination of ispinesib and capecitabine may have an acceptable tolerability profile. The optimally tolerated regimen in this clinical trial was not defined at that time; however, the MTD of ispinesib as monotherapy (18 mg/m<sup>2</sup>, administered as an intravenous infusion every 21 days) was tolerated with therapeutic doses of capecitabine, specifically daily oral doses of 2000 mg/m<sup>2</sup> and 2500 mg/m<sup>2</sup> for 14 days. Plasma concentrations of ispinesib did not appear to be affected by the presence of capecitabine. Dose-limiting toxicities consisted of Grade 2 rash that did not allow 75% of the capecitabine doses to be delivered and prolonged Grade 4 neutropenia. In this clinical trial, a total of 12 out of 24 patients had a best response of stable disease as determined by RECIST. We anticipate final data

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from this clinical trial to be available in the first half of 2008. The timing of availability of these data is based on information provided by GSK and is outside of our control.

*Pediatric Solid Tumors:* The NCI continues to conduct a Phase I clinical trial designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of ispinesib as monotherapy administered as a one-hour infusion on days 1, 8 and 15 of a 28-day schedule to pediatric patients with relapsed or refractory solid tumors.

*Acute Leukemias, Chronic Myelogenous Leukemia or Advanced Myelodysplastic Syndromes:* The NCI has closed enrollment in a Phase I clinical trial designed to evaluate the safety, tolerability and pharmacokinetic profile of ispinesib as monotherapy administered as a one-hour infusion on days 1, 2 and 3 of a 21-day cycle in adult patients with relapsed or refractory acute leukemias, chronic myelogenous leukemia in blast crisis or advanced myelodysplastic syndromes.

*Preclinical Research:* At the 2007 Annual Meeting of the American Association for Cancer Research, or AACR, a poster was presented containing data from non-clinical studies designed to examine whether spindle disruption by inhibition of KSP with ispinesib may have therapeutic potential in the treatment of multiple myeloma. The authors concluded that KSP inhibition with ispinesib was able to induce growth arrest and cell death in myeloma cells, and overcome resistance to both conventional drugs and novel agents, such as bortezomib. They also concluded that ispinesib's preferential activity against transformed plasma cells with the sparing of normal bone marrow cells provides a rationale for the clinical development of ispinesib as a potential treatment for relapsed or refractory multiple myeloma.

We expect that it will take several years before we can commercialize ispinesib, if at all. Ispinesib is at too early a stage of development for us to predict if and when we will be in a position to generate any revenues or material net cash flows from any resulting drugs. Accordingly, we cannot reasonably estimate when and to what extent ispinesib will generate revenues or material net cash flows, which may vary widely depending on numerous factors, including, but not limited to, the safety and efficacy profile of the drug, receipt of regulatory approvals, market acceptance, then-prevailing reimbursement policies, competition and other market conditions. We have assumed responsibility for funding the research and development costs associated with ispinesib pursuant to the November 2006 amendment to the GSK Agreement. We have initiated a focused development program for ispinesib in the treatment of patients with locally advanced or metastatic breast cancer designed to further define the clinical activity profile of ispinesib in advanced breast cancer patients, and in preparation for potentially initiating a Phase III clinical trial of ispinesib for the second-line treatment of advanced breast cancer. As a result of this planned development activity, or if GSK does not exercise its option to resume responsibility for some or all of the development and commercialization activities associated with this drug candidate, our expenditures relating to research and development of this drug candidate will increase significantly.

**SB-743921**

SB-743921, our second anti-cancer drug candidate, also inhibits KSP but is structurally distinct from ispinesib. SB-743921 is also being developed in connection with our strategic alliance with GSK. Though we are aware of no clinical shortcomings of ispinesib that are addressed by SB-743921, we believe that having two KSP inhibitors in concurrent clinical development increases the likelihood that a commercial product will result from this research and development program.

SB-743921 was studied by GSK in a dose-escalating Phase I clinical trial evaluating its safety, tolerability and pharmacokinetics in advanced cancer patients. The primary objectives of this clinical trial were to determine the dose limiting toxicities, or DLTs, and to establish the MTD of SB-743921 administered intravenously on a once every 21-day schedule. Secondary objectives included assessment of the safety and tolerability of SB-743921,

characterization of the pharmacokinetics of SB-743921 on this schedule and a preliminary assessment of its anti-tumor activity. The observed toxicities at the recommended Phase II dose were manageable. DLTs in this clinical trial consisted predominantly of neutropenia and elevations in hepatic enzymes and bilirubin. Disease stabilization, ranging from 9 to 45 weeks, was observed in seven patients. One patient with cholangiocarcinoma had a confirmed partial response at the MTD.

In 2006, we initiated, at our expense, an additional clinical trial of SB-743921 in hematologic cancers. We continue to enroll and dose-escalate patients in an open-label, non-randomized Phase I/II clinical trial to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of SB-743921 administered as a one-hour

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infusion on days 1 and 15 of a 28-day schedule in patients with Hodgkin or non-Hodgkin lymphoma. In December 2007, at the Annual Meeting of the American Society of Hematology, a poster was presented summarizing interim data from Phase I of this clinical trial. The authors concluded that SB-743921 is well-tolerated without prophylactic granulocyte-colony stimulating factor at doses less than 6 mg/m<sup>2</sup> when given on this alternative dosing schedule. The best response observed was a partial response in a patient with Hodgkin lymphoma at 6 mg/m<sup>2</sup>. In this interim analysis, Grade 3 or 4 neutropenia was the most common toxicity reported and Grade 3 or 4 non-hematological toxicities have been rare. In particular, there has been no evidence of neuropathy. We anticipate final data to be available from the Phase I portion of this trial in the first half of 2008.

The clinical trials program for SB-743921 may proceed for several years, and we will not be in a position to generate any revenues or material net cash flows from this drug candidate until the program is successfully completed, regulatory approval is achieved, and a drug is commercialized. SB-743921 is at too early a stage of development for us to predict when or if this may occur. The November 2006 amendment to the GSK Agreement provides for us to fund the future development of SB-743921 in all cancer indications subject to GSK's option to resume responsibility for some or all development and commercialization activities. As a result of our conduct of our current Phase I/II clinical trial of SB-743921 in hematologic cancers, and any further development activities for SB-743921 we may conduct under this amendment, our expenditures relating to research and development of this drug candidate will increase significantly.

If GSK exercises its option for either or both of ispinesib and SB-743921, it will pay us an option fee equal to the costs we independently incurred for the development of that drug candidate, plus a premium intended to compensate us for the cost of capital associated with such costs, subject to an agreed limit for such costs and premium. Upon GSK exercising its option for a drug candidate, we may receive additional pre-commercialization milestone payments with respect to such drug candidate and increased royalties on net sales of any resulting product, in each case, beyond those contemplated under the original agreement.

**GSK-923295**

GSK-923295 is the third drug candidate to arise from our strategic alliance with GSK. GSK-923295 is an inhibitor of a second mitotic kinesin, centromere-associated protein E, or CENP-E. CENP-E is directly involved in coordinating the decision a cell makes to divide with the actual trigger of the mechanics of cell division. These processes are essential for cancer cells to grow. GSK-923295 causes partial and complete shrinkages of human tumors in animal models and has exhibited properties in these studies that distinguish it from ispinesib and SB-743921.

In August 2007, we announced that GSK had initiated a first-time-in-humans Phase I clinical trial of GSK-923295. This Phase I clinical trial is an open-label, non-randomized, dose-finding trial designed to investigate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of GSK-923295 in patients with advanced solid tumors. The initiation of this clinical trial triggered a milestone payment of \$1.0 million from GSK to Cytokinetics under the GSK Agreement. We anticipate data to be available from this clinical trial in 2008. The timing of availability of these data is based on information provided by GSK and is outside of our control.

Preclinical data relating to GSK-923295 were presented in two posters at the April 2007 Annual Meeting of the AACR. The authors of one poster concluded that GSK-923295, a potent and selective inhibitor of CENP-E, elicited a dose-dependent response against a wide variety of human tumor xenografts models in nude mice. Tumor regression was observed in seven of eleven of the models studied. The mechanism of cell cycle arrest was consistent with that observed in cell culture, as judged by histological examination of tumors in a colon cancer xenograft. The authors of the second poster, a biochemical analysis of GSK-923295, described its unique mechanism of CENP-E inhibition. This biochemical mechanism of action is consistent with the cellular response and clearly distinguishable from the mitotic kinesin inhibitors ispinesib and monastrol.

In October 2007, at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, two posters related to GSK-923295 were presented. The first poster described the antiproliferative activity of GSK-923295 across a panel of 214 solid and 85 hematological tumor cell lines. Activity was not limited to any one tumor type and only four of the cell lines tested were fully resistant to treatment with our CENP-E inhibitor. In a second poster, the molecular basis for response to GSK-923295 was characterized across a series of cell lines with varying sensitivity and related to the mitotic checkpoint and programmed cell death machinery.



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The development program for GSK-923295 may proceed for several years, and we will not be in a position to generate any revenues or material net cash flows from this potential drug candidate unless the program is successfully completed, regulatory approval is achieved and a drug is commercialized. GSK-923295 is at too early a stage of development for us to predict when or if this may occur. If GSK abandons development of GSK-923295 prior to regulatory approval, we may undertake and fund the clinical development of this drug candidate, or its commercialization, or we may seek a new partner for such clinical development or commercialization, or curtail or abandon such clinical development.

Ispinesib, SB-743921 and GSK-923295 are being developed in connection with the GSK Agreement, executed in 2001. This strategic alliance is directed to the discovery, development and commercialization of novel small molecule drugs targeting KSP, CENP-E and certain other mitotic kinesins for applications in the treatment of cancer and other diseases. Under our strategic alliance, GSK, in collaboration with the NCI, conducted a broad Phase II clinical trials program designed to evaluate ispinesib across multiple tumor types, as well as a Phase I clinical trial of SB-743921. Pursuant to a November 2006 amendment to the GSK Agreement, we assumed responsibility, at our expense, for the continued research, development and commercialization of ispinesib and SB-743921, subject to GSK's option to resume development and commercialization of either or both of ispinesib and SB-743921. This option is exercisable during a defined period. GSK is currently conducting a Phase I clinical trial of GSK-923295. In June 2007, we amended the GSK Agreement to extend the research term for an additional year through June 19, 2008 to facilitate continued research activities under an updated research plan focused on CENP-E. Under the June 2007 amendment, GSK will have no obligation to reimburse us for full-time employee equivalents, or FTEs, during the extension of the research term. For those drug candidates that GSK develops under the strategic alliance, we can elect to co-fund certain later-stage development activities which would increase our potential royalty rates on sales of resulting drugs and provide us with the option to secure co-promotion rights in North America. If we elect to co-fund later-stage development, we expect that the royalties to be paid on future sales of each of ispinesib, SB-743921 and GSK-923295 could potentially increase to an upper-teen percentage rate based on increasing product sales and our anticipated level of co-funding. If we exercise our co-promotion option, then we are entitled to receive reimbursement from GSK for certain sales force costs we incur in support of our commercial activities.

We recorded research and development expenses for activities relating to our mitotic kinesin programs of approximately \$5.8 million, \$6.1 million, and \$8.6 million in the years ended December 31, 2007, 2006 and 2005, respectively. We anticipate that our expenditures relating to the development of ispinesib and SB-743921 will increase significantly as we advance through clinical development. Our expenditures will also increase if GSK does not exercise its option to resume responsibility for some or all of the development and commercialization activities associated with ispinesib and SB-743921, or if we elect to co-fund later-stage development for one or more of ispinesib, SB-743921 and GSK-923295. For those drug candidates and potential drug candidates that GSK develops under the strategic alliance, which currently includes GSK-923295 and which may include either or both of ispinesib and SB-743921 if so elected by GSK pursuant to its option, we may elect to co-fund certain later-stage development activities which would increase our potential royalty rates on sales of resulting drugs and provide us with the option to secure co-promotion rights in North America. We expect that the royalties to be paid on potential future sales, if any, by GSK of each of ispinesib, SB-743921 and GSK-923295 will be based on increasing product sales and our anticipated level of co-funding, if any. If we exercise our co-promotion option, then we will receive reimbursement from GSK for certain sales force costs we incur in support of our commercial activities.

## **Development Risks**

The successful development of all of our drug candidates is highly uncertain. We cannot estimate with certainty or know the exact nature, timing and estimated costs of the activities necessary to complete the development of any of our drug candidates or the date of completion of these development activities. We cannot estimate with certainty any of the foregoing due to the numerous risks and uncertainties associated with developing our drug candidates,

including, but not limited to:

the uncertainty of the timing of the initiation and completion of patient enrollment in our clinical trials;

the possibility of delays in the collection of clinical trial data and the uncertainty of the timing of the analyses of our clinical trial data after such trials have been initiated and completed;

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the possibility of delays in characterization, synthesis or optimization of potential drug candidates in our cardiovascular program;

delays or additional costs in developing appropriate formulations of our drug candidates for clinical trial use;

the uncertainty of clinical trial results;

the uncertainty of obtaining FDA or other foreign regulatory agency approval required for the clinical investigation of new therapies; and

the uncertainty related to the development of commercial scale manufacturing processes and qualification of a commercial scale manufacturing facility.

If we fail to complete the development of any of our drug candidates in a timely manner, it could have a material adverse effect on our operations, financial position and liquidity. In addition, any failure by us or our partners to obtain, or any delay in obtaining, regulatory approvals for our drug candidates could have a material adverse effect on our results of operations. A further discussion of the risks and uncertainties associated with completing our programs on schedule, or at all, and certain consequences of failing to do so are discussed further in the risk factors entitled "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," "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" and "Clinical trials are expensive, time consuming and subject to delay," as well as other risk factors.

**Revenues**

Our current revenue sources are limited, and we do not expect to generate any direct revenue from product sales for several years. We have recognized revenues from our strategic alliances with Amgen, GSK and AstraZeneca for license fees and contract research activities.

Under the terms of our collaboration and option agreement with Amgen, or the Amgen Agreement, we received an upfront, non-refundable license and technology access fee of \$42.0 million. In connection with entering into the collaboration and option agreement, we also entered into a common stock purchase agreement, or the CSPA, with Amgen. In January 2007, we issued 3,484,806 shares of our common stock to Amgen for net proceeds of \$32.9 million, of which the \$6.9 million purchase premium was recorded as deferred revenue. We are amortizing the upfront fee and stock premium to license revenue ratably over the maximum term of the non-exclusive license, which is four years. We may receive additional payments from Amgen upon achieving certain precommercialization and commercialization milestones. Milestone payments are non-refundable and are recognized as revenue when earned, as evidenced by achievement of the specified milestones and the absence of ongoing performance obligations.

We may also be eligible to receive reimbursement for contract development activities subsequent to Amgen's option exercise, which we will record as revenue if and when the related expenses are incurred. We record amounts received in advance of performance as deferred revenue.

Charges to GSK in 2006 were based on negotiated rates intended to approximate the costs for our FTEs performing research under the strategic alliance and our out-of-pocket expenses, which we recorded as the related expenses were incurred. GSK paid us an upfront licensing fee, which we recognized ratably over the strategic alliance's initial five-year research term, which ended in June 2006. In 2007, we received a \$1.0 million milestone payment from GSK relating to its initiation of a phase I clinical trial of GSK-295. We may receive additional payments from GSK upon

achieving certain precommercialization milestones. Milestone payments are non-refundable and are recognized as revenue when earned, as evidenced by achievement of the specified milestones and the absence of ongoing performance obligations. We record amounts received in advance of performance as deferred revenue. The revenues recognized to date are not refundable, even if the relevant research effort is not successful.

Charges to AstraZeneca in 2005 were based on negotiated rates intended to approximate the costs for our FTEs performing research under the strategic alliance. The revenues recognized since inception to date are not refundable. The research term of our collaboration and license agreement with AstraZeneca expired in December 2005, and we formally terminated that agreement in August 2006.

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Because a substantial portion of our revenues for the foreseeable future will depend on achieving development and other precommercialization milestones under our strategic alliances with GSK and Amgen, our results of operations may vary substantially from year to year.

We expect that our future revenues will most likely be derived from royalties on sales from drugs licensed to GSK or Amgen under our strategic alliances and from those licensed to future partners, as well as from direct sales of our drugs. If Amgen exercises its option, we will retain a product-by-product option to co-fund certain later-stage development activities under our strategic alliance with Amgen, thereby potentially increasing our royalties and affording us co-promotion rights in North America. For those products being developed by GSK under our strategic alliance, we also retain a product-by-product option to co-fund certain later-stage development activities, thereby potentially increasing our royalties and affording us co-promotion rights in North America. If we exercise our co-promotion rights under either strategic alliance, we are entitled to receive reimbursement for certain sales force costs we incur in support of our commercial activities.

## **Research and Development**

We incur research and development expenses associated with both partnered and unpartnered research activities, as well as the development and expansion of our drug discovery technologies. Research and development expenses related to our strategic alliance with GSK consisted primarily of costs related to research and screening, lead optimization and other activities relating to the identification of compounds for development as mitotic kinesin inhibitors for the treatment of cancer. Prior to June 2006, certain of these costs were reimbursed by GSK on an FTE basis. From 2001 through November 2006, GSK funded the majority of the costs related to the clinical development of ispinesib and SB-743921. Under our November 2006 amendment to the GSK Agreement, we assumed responsibility for the continued research, development and commercialization of inhibitors of KSP, including ispinesib and SB-743921, and other mitotic kinesins, at our sole expense subject to GSK's option to resume responsibility for the development and commercialization of either or both of ispinesib and SB-743921, exercisable during a defined period. We also have the option to co-fund certain later-stage development activities for GSK-923295. This commitment and the potential exercise of our co-funding option will result in a significant increase in research and development expenses. We expect to incur research and development expenses in the continued conduct of preclinical studies and clinical trials for CK-1827452 and other of our cardiac myosin activator compounds for the treatment of heart failure and in connection with our early research programs in other diseases, as well as the continued refinement and application of our existing and future proprietary drug discovery technologies. Research and development expenses related to any development and commercialization activities we elect to fund would consist primarily of employee compensation, supplies and materials, costs for consultants and contract research, facilities costs and depreciation of equipment. From our inception through December 31, 2007, we incurred costs of approximately \$60.2 million for research and development activities relating to the discovery of mitotic kinesin inhibitors, \$104.0 million for our cardiac contractility program, \$49.9 million for our proprietary technologies and \$69.4 million for all other programs.

## **General and Administrative Expenses**

General and administrative expenses consist primarily of compensation for employees in executive and administrative functions, including, but not limited to, finance, human resources, legal, business and commercial development and strategic planning. Other significant costs include facilities costs and professional fees for accounting and legal services, including legal services associated with obtaining and maintaining patents. We anticipate continued increases in general and administrative expenses associated with operating as a publicly traded company.

**Table of Contents****Stock Compensation**

The following table summarizes stock-based compensation related to employee stock options and employee stock purchases for 2007 and 2006, which was allocated as follows (in thousands):

|   | <b>Years Ended<br/>December 31,</b> |             |
|---|-------------------------------------|-------------|
|   | <b>2007</b>                         | <b>2006</b> |
| Research and development                                | \$ 2,932                            | \$ 2,532    |
| General and administrative                              | 2,621                               | 2,111       |
| Stock-based compensation included in operating expenses | \$ 5,553                            | \$ 4,643    |

As of December 31, 2007, there was \$10.3 million of total unrecognized compensation cost related to non-vested stock-based compensation arrangements granted under our stock option plans. That cost is expected to be recognized over a weighted-average period of 2.6 years. In addition, we continue to amortize deferred stock-based compensation recorded prior to adoption of Statement of Financial Accounting Standards, or SFAS, No. 123R, for stock options granted prior to the initial public offering. At December 31, 2007, the balance of deferred stock based compensation was \$0.3 million, which we expect to amortize to expense in 2008.

**Income Taxes**

We account for income taxes in accordance with SFAS 109, *Accounting for Income Taxes*, which is the asset and liability method for accounting and reporting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized. We have not recorded an income tax provision in the years ended December 31, 2007, 2006 and 2005 because we had a net taxable loss in each of those periods. Given that we have a history of recurring losses, we have recorded a full valuation allowance against our deferred tax assets. We had federal net operating loss carryforwards of approximately \$265.2 million and state net operating loss carryforwards of approximately \$95.1 million at December 31, 2007. The federal and state operating loss carryforwards will begin to expire in 2018 and 2008, respectively, if not utilized. The net operating loss carryforwards include deductions for stock options. When utilized, the portion related to stock options deductions will be accounted for as a credit to stockholders' equity rather than as a reduction of the income tax provision.

We had research credit carryforwards of approximately \$7.5 million and \$9.1 million for federal and state income tax purposes, respectively, at December 31, 2007. If not utilized, the federal carryforwards will expire in various amounts beginning in 2018. The California state credit can be carried forward indefinitely.

The Tax Reform Act of 1986 limits the use of net operating loss and tax credit carryforwards in certain situations where equity transactions resulted in a change of ownership as defined by Internal Revenue Code Section 382. During the year ended December 31, 2007, we conducted a study and determined that our use of our federal research credit is subject to such a restriction. Accordingly, we reduced its deferred tax assets and the corresponding valuation allowance by \$0.8 million. As a result, the research credit amount as of December 31, 2007 reflects the restriction on our ability to use the credit.

On January 1, 2007, we adopted the provisions of Financial Accounting Standards Board, or FASB, Interpretation No. 48, or FIN 48, *Accounting for Uncertainty in Income Taxes, an interpretation of SFAS 109*. The new standard defines the threshold for recognizing the benefits of tax return positions in the financial statements as

more-likely-than-not to be sustained by the taxing authorities based solely on the technical merits of the position. If the recognition threshold is met, the tax benefit is measured and recognized as the largest amount of tax benefit, in our judgment, which is greater than 50% likely to be realized. The cumulative effect of adopting FIN 48 on January 1, 2007 resulted in no FIN 48 liability on the balance sheet. The total amount of unrecognized tax benefits as of the date of adoption was \$3.1 million. We are currently not subject to income tax examinations and, in general, all tax years remain open due to net operating losses.

Interest and penalties are zero, and our policy to account for interest and penalties is to classify both as income tax expense in the financial statements. Because we have recorded a full valuation allowance on all our deferred tax

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assets, FIN 48 has had no impact on our effective tax rate. We do not expect our unrecognized tax benefits to change materially over the next 12 months.

**Interest and Other Income and Expense**

Interest and other income and expense consist primarily of interest income and interest expense. Interest income is primarily generated from our cash, cash equivalents and investments. Interest expense generally relates to the borrowings under our equipment financing lines.

**Results of Operations*****Years ended December 31, 2007, 2006 and 2005******Revenues***

|  | Years Ended   |        |        | Increase   |          |
|--|---------------|--------|--------|------------|----------|
|  | December 31,  |        |        | (Decrease) |          |
|  | 2007          | 2006   | 2005   | 2007       | 2006     |
|  | (In millions) |        |        |            |          |
| Research and development revenues from related party | \$ 1.4        | \$ 1.6 | \$ 5.0 | \$ (0.2)   | \$ (3.4) |
| Research and development, grant and other revenues   |               |        | 1.1    |            | (1.1)    |
| License revenues from related parties                | 12.2          | 1.5    | 2.8    | 10.7       | (1.3)    |
| Total revenues                                       | \$ 13.6       | \$ 3.1 | \$ 8.9 | \$ 10.5    | \$ (5.8) |

We recorded total revenues of \$13.6 million, \$3.1 million and \$8.9 million for the years ended December 31, 2007, 2006 and 2005, respectively.

Research and development revenues from related party refers to revenues from our partner GSK, which is also a stockholder of the Company. Research and development revenues from GSK of \$1.4 million in 2007 consisted of a \$1.0 milestone payment for GSK's initiation of a Phase I clinical trial of GSK-923295 in patients with solid tumors, and patent expense reimbursements of \$0.4 million. Research and development revenues from GSK of \$1.6 million in 2006 consisted of \$1.4 million for the reimbursement of FTEs and approximately \$0.2 million for patent expense reimbursements. Research and development revenues from GSK of \$5.0 million in 2005 consisted of \$3.8 million for the reimbursement of FTEs, \$0.5 million for milestone revenues and \$0.7 million for patent expense reimbursements. The \$0.5 million milestone revenue received from GSK in 2005 related to the GSK's selection of GSK-923295 as a development compound under our strategic alliance in the fourth quarter of 2005.

FTE reimbursements from GSK terminated in June 2006 due to the conclusion of the research term under the GSK Agreement for all mitotic kinesins except CENP-E. FTE reimbursements also decreased in 2006 compared to 2005 as the result of a contractually pre-defined change in FTE sponsorship. The FTE sponsorship was determined annually by GSK and us in accordance with the annual research plan and contractually predefined FTE support levels. In June 2006, the five-year research term of our strategic alliance with GSK was extended for an additional year under an updated research plan focused only on CENP-E without corresponding FTE reimbursement.



Research and development, grant and other revenues of \$1.1 million for the year ended December 31, 2005 consisted entirely of reimbursement for FTEs from AstraZeneca under our strategic alliance. The research term of our collaboration and license agreement with AstraZeneca expired in December 2005, and we formally terminated that agreement in August 2006.

License revenues from related parties represents license revenue from our strategic alliances with Amgen and GSK. License revenue from Amgen was \$12.2 million in 2007 and \$0.1 million in 2006, and represented recognition of the upfront license fee and the premium paid on the common stock purchase by Amgen. As of December 31, 2007, our remaining balance of Amgen deferred revenue was \$36.6 million. We are amortizing the Amgen deferred revenue on a straight-line basis over the maximum term of the non-exclusive license granted to Amgen under the collaboration and option agreement, which is four years. License revenue from GSK was zero in 2007, \$1.4 million in 2006 and \$2.8 million in 2005. The license revenue from GSK was amortized on a straight-line basis over the agreement's initial research term, which ended in June 2006.

We anticipate total revenues for the year ending December 31, 2008 to be approximately \$12.0 million.

**Table of Contents***Research and development expenses*

|                                   | Years Ended December 31, |         |         | Increase<br>(Decrease) |        |
|-----------------------------------|--------------------------|---------|---------|------------------------|--------|
|                                   | 2007                     | 2006    | 2005    | 2007                   | 2006   |
|                                   | (In millions)            |         |         |                        |        |
| Research and development expenses | \$ 53.4                  | \$ 49.2 | \$ 40.6 | \$ 4.2                 | \$ 8.6 |

Research and development expenses increased \$4.2 million in 2007 compared to 2006, and increased \$8.6 million in 2006 compared to 2005. The increase in 2007 was primarily due to increases of \$2.5 million related to our cardiovascular and oncology clinical trial programs and preclinical outsourcing costs, \$1.5 million for personnel expenses and \$0.3 million for facilities expenses. The increase in research and development expenses in 2006, compared to 2005, was primarily due to increases in outsourcing costs related to the manufacture of clinical supplies and for our cardiovascular and oncology clinical trial programs of \$4.0 million, laboratory facilities and lab consumables expense of \$2.0 million, and compensation and benefit related costs of \$2.6 million.

From a program perspective, the increase in research and development spending in 2007, compared to 2006, was due to increases of \$4.3 million for our cardiac contractility program and \$2.1 million for our early research programs, partially offset by decreases in spending for mitotic kinesin inhibitors of \$0.3 million and for our proprietary technologies of \$1.9 million. In 2006, from a program perspective, the increased research and development spending, compared to 2005, was primarily due to increased spending on our early research programs partially offset by slight decreases in spending on oncology and cardiovascular programs and proprietary technologies.

|   | Years Ended December 31, |         |         | Increase<br>(Decrease) |          |
|---|--------------------------|---------|---------|------------------------|----------|
|   | 2007                     | 2006    | 2005    | 2007                   | 2006     |
|   | (In millions)            |         |         |                        |          |
| Mitotic kinesin inhibitors              | \$ 5.8                   | \$ 6.1  | \$ 8.6  | \$ (0.3)               | \$ (2.5) |
| Cardiac contractility                   | 22.4                     | 18.1    | 19.6    | 4.3                    | (1.5)    |
| Proprietary technologies                | 3.9                      | 5.8     | 6.4     | (1.9)                  | (0.6)    |
| All other research programs             | 21.3                     | 19.2    | 6.0     | 2.1                    | 13.2     |
| Total research and development expenses | \$ 53.4                  | \$ 49.2 | \$ 40.6 | \$ 4.2                 | \$ 8.6   |

For the years ended December 31, 2007, 2006 and 2005, GSK reimbursed costs of \$0.4 million, \$1.6 million and \$4.5 million, respectively, of research and development activities relating to the discovery of mitotic kinesin inhibitors. We recorded these reimbursements as related party revenue.

Clinical timelines, likelihood of success and total completion costs vary significantly for each drug candidate and are difficult to estimate. We anticipate that we will make determinations as to which early research programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each drug candidate. The lengthy process of seeking regulatory approvals and subsequent compliance with applicable regulations requires the expenditure of substantial resources. Any failure by us to obtain and maintain, or any delay in obtaining, regulatory approvals could cause our research and development expenditures to increase and,

in turn, could have a material adverse effect on our results of operations.

We expect research and development expenditures to continue to increase in 2008. We expect to advance research and development of our drug candidate CK-1827452 for the potential treatment of heart failure and our drug candidates ispinesib and SB-743921 for the potential treatment of cancer. We anticipate research and development expenses to be in the range of \$62.0 million to \$67.0 million for 2008.

*General and administrative expenses*

|                                     | <b>Years Ended<br/>December 31,</b> |             |             | <b>Increase<br/>(Decrease)</b> |             |
|-------------------------------------|-------------------------------------|-------------|-------------|--------------------------------|-------------|
|                                     | <b>2007</b>                         | <b>2006</b> | <b>2005</b> | <b>2007</b>                    | <b>2006</b> |
|                                     | <b>(In millions)</b>                |             |             |                                |             |
| General and administrative expenses | \$ 16.7                             | \$ 15.2     | \$ 13.0     | \$ 1.5                         | \$ 2.2      |

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General and administrative expenses increased \$1.5 million in 2007, compared with 2006, and increased \$2.2 million in 2006, compared with 2005. The increase in general and administrative expenses in 2007 was primarily due to increases in personnel expenses of \$1.5 million, outside services, including audit, accounting and tax fees, of \$0.4 million, and facilities costs of \$0.4 million. These increases were partially offset by a \$0.8 million decrease in legal expenses. The increase in general and administrative expenses in 2006, compared to 2005, was primarily due to increased expenses related to compensation and benefits of \$2.2 million and higher legal fees of \$0.1 million, partially offset by lower outsourcing costs of \$0.1 million.

We expect that general and administrative expenses will continue to increase during 2008 due to higher payroll-related expenses in support of our continuing corporate development activities, business development costs, expanding operational infrastructure, and costs associated with being a public company. We anticipate general and administrative expenses to be in the range of \$20.0 million to \$22.0 million for 2008.

*Interest and Other Income and Expense*

|                            | Years Ended<br>December 31, |          |          | Increase<br>(Decrease) |        |
|----------------------------|-----------------------------|----------|----------|------------------------|--------|
|                            | 2007                        | 2006     | 2005     | 2007                   | 2006   |
|                            | (In millions)               |          |          |                        |        |
| Interest and other income  | \$ 8.3                      | \$ 4.7   | \$ 2.9   | \$ 3.6                 | \$ 1.8 |
| Interest and other expense | \$ (0.7)                    | \$ (0.5) | \$ (0.5) | \$ 0.2                 | \$     |

Interest and other income consists primarily of interest income generated from our cash, cash equivalents and investments. The increase in interest and other income in 2007, compared to 2006, was primarily due to higher average balances of cash, cash equivalents and short-term investments, whereas the increase in 2006, compared with 2005, was primarily due to higher market interest rates earned on our invested cash.

Interest and other expense primarily consists of interest expense on borrowings under our equipment financing lines. The increase in interest and other expense in 2007 compared to 2006, was due to higher average effective interest rates as well as higher average outstanding balances. The total balance outstanding under our equipment financing lines was \$8.7 million at December 31, 2007 and \$10.8 million at December 31, 2006, respectively.

**Liquidity and Capital Resources**

From August 5, 1997, our date of inception, through December 31, 2007, we funded our operations through the sale of equity securities, equipment financings, non-equity payments from collaborators, government grants and interest income.

Our cash, cash equivalents and investments, excluding restricted cash, totaled \$139.8 million at December 31, 2007, an increase of \$30.3 million from \$109.5 million at December 31, 2006. The increase was primarily due to the receipt of the \$42.0 million upfront license fee from Amgen in January 2007, net proceeds of \$32.9 million from the issuance of common stock to Amgen in January 2007, and proceeds of \$9.5 million from the issuance of stock under the committed equity financing facility, or CEFF, with Kingsbridge Capital Limited, or Kingsbridge, in 2005. The increases were partially offset by the use of cash to fund operations.

We have received net proceeds from the sale of equity securities of \$314.7 million from August 5, 1997, the date of our inception, through December 31, 2007, excluding sales of equity to GSK and Amgen. Included in these proceeds

are \$94.0 million received upon closing of the initial public offering of our common stock in May 2004. In 2001, in connection with the GSK Agreement, GSK made a \$14.0 million equity investment in the Company. GSK made additional equity investments in the Company in 2003 and 2004 of \$3.0 million and \$7.0 million, respectively.

In 2005, we entered into the 2005 CEFF, pursuant to which Kingsbridge committed to finance up to \$75.0 million of capital for a three-year period. Subject to certain conditions and limitations, from time to time under the 2005 CEFF, at our election, Kingsbridge purchased newly-issued shares of our common stock at a price between 90% and 94% of the volume weighted average price on each trading day during an eight day, forward-looking pricing period. We received gross proceeds from draw downs and sales of our common stock to Kingsbridge under the 2005 CEFF as follows: 2005 gross proceeds of \$5.7 million from the sale of 887,576 shares, before offering costs of \$178,000; 2006 gross proceeds of \$17.0 million from the sale of 2,740,735 shares; and

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2007 gross proceeds of \$9.5 million from the sale of 2,075,177 shares. No further draw downs are available to us under the 2005 CEFF with Kingsbridge.

In October 2007, we entered into a new CEFF with Kingsbridge, or the 2007 CEFF, pursuant to which Kingsbridge committed to finance up to \$75.0 million of capital for a three-year period. Subject to certain conditions and limitations, from time to time under the 2007 CEFF, at our election, Kingsbridge is committed to purchase newly-issued shares of our common stock at a price between 90% and 94% of the volume weighted average price on each trading day during an eight day, forward-looking pricing period. The maximum number of shares we may issue in any pricing period is the lesser of 2.5% of our market capitalization immediately prior to the commencement of the pricing period or \$15.0 million. As part of the arrangement, we issued a warrant to Kingsbridge to purchase 230,000 shares of our common stock at a price of \$7.99 per share, which represents a premium over the closing price of our common stock on the date we entered into the 2007 CEFF. This warrant is exercisable beginning six months after the date of grant and for a period of three years thereafter. Under the terms of the 2007 CEFF, the maximum number of shares we may sell is 9,779,411 (exclusive of the shares underlying the warrant) which, under the rules of the NASDAQ Stock Market LLC, is approximately the maximum number of shares we may sell to Kingsbridge without approval of our stockholders. This limitation may further limit the amount of proceeds we are able to obtain from the 2007 CEFF. We are not obligated to sell any of the \$75.0 million of common stock available under the 2007 CEFF and there are no minimum commitments or minimum use penalties. The 2007 CEFF does not contain any restrictions on our operating activities, any automatic pricing resets or any minimum market volume restrictions. To date we have made no draw downs under the 2007 CEFF with Kingsbridge.

In January 2006, we entered into a stock purchase agreement with certain institutional investors relating to the issuance and sale of 5,000,000 shares of our common stock at a price of \$6.60 per share, for gross offering proceeds of \$33.0 million. In connection with this offering, we paid an advisory fee to a registered broker-dealer of \$1.0 million. After deducting the advisory fee and the offering costs, we received net proceeds of approximately \$32.0 million from the offering.

In December 2006, we entered into stock purchase agreements with selected institutional investors relating to the issuance and sale of 5,285,715 shares of our common stock at a price of \$7.00 per share, for gross offering proceeds of \$37.0 million. In connection with this offering, we paid placement agent fees to three registered broker-dealers totaling \$1.9 million. After deducting the placement agent fees and the offering costs, we received net proceeds of approximately \$34.9 million from the offering.

In connection with our entry into the collaboration and option agreement with Amgen, we entered into a common stock purchase agreement under which Amgen purchased 3,484,806 shares of our common stock at a price per share of \$9.47, including a premium of \$1.99 per share, and an aggregate purchase price of approximately \$33.0 million. After deducting the offering costs, we received net proceeds of approximately \$32.9 million. These shares were issued, and the related proceeds received, in January 2007.

As of December 31, 2007, we have received \$54.3 million in non-equity payments from GSK and \$42.0 million in non-equity payments from Amgen.

We received \$1.7 million, \$4.3 million and \$1.3 million under equipment financing arrangements in 2007, 2006 and 2005, respectively. Interest earned on investments, excluding non-cash amortization of purchase premiums, in the years ended December 31, 2007, 2006 and 2005 was \$4.6 million, \$2.7 million and \$3.8 million, respectively.

Net cash used in operating activities was \$3.0 million in 2007 and primarily resulted from the our net loss of \$48.9 million, partially offset by the receipt from Amgen in January 2007 of the \$42.0 million upfront, non-refundable license and technology access fee under the collaboration and option agreement entered into in December 2006.

Deferred revenue decreased \$5.3 million in 2007 to \$36.6 million at December 31, 2007 from \$41.9 million at December 31, 2006. The decrease was due to the \$12.2 million amortization of deferred Amgen license revenue, partially offset by a \$6.9 million increase in January 2007 resulting from the premium paid by Amgen for the purchase of stock under the CSPA.

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Net cash provided by investing activities was \$45.5 million in 2007 and primarily represented proceeds from the maturity of investments, net of investment purchases, of \$47.0 million, partly offset by funds used to purchase property and equipment of \$2.6 million. Net cash used in investing activities of \$13.7 million for the year ended December 31, 2006 was primarily due to net purchases of investments in addition to property and equipment purchases. Cash provided by investing activities of \$34.5 million for the year ended December 31, 2005 was primarily due to net proceeds from sales and maturities of investments, slightly offset by \$1.5 million of property and equipment purchases.

Restricted cash totaled \$5.2 million, \$6.0 million and \$5.2 million at December 31, 2007, 2006 and 2005, respectively. Restricted cash decreased in 2007 due to the lower security deposit required by our lender, consistent with the decrease in the outstanding balance under our equipment financing line of credit. Restricted cash increased in 2006 consistent with an increase in the balance outstanding under our equipment financing line of credit, net of a reduction in the security deposit required by our lender.

Net cash provided by financing activities was \$34.7 million, \$86.7 million and \$5.4 million for the years ended December 31, 2007, 2006 and 2005, respectively. Net cash provided by financing activities in 2007 primarily represented net proceeds of approximately \$32.9 million from the issuance of common stock to Amgen, less \$6.9 million that was recorded as deferred revenue, and \$9.5 million gross proceeds from the issuance of stock under the 2005 CEFF. Net cash provided by financing activities in 2006 was primarily due to net proceeds from our two public offerings of \$66.9 million, proceeds from draw down of the 2005 CEFF of \$17.0 million and proceeds from equipment financing lines of \$4.3 million. Net cash provided by financing activities in 2005 was primarily due to net proceeds from draw down of the 2005 CEFF of \$5.5 million and proceeds of approximately \$1.1 million from the issuance of common stock associated with our employee stock plans, partially offset by an overall decrease in our equipment financing line of \$1.1 million.

Investments as of December 31, 2007 consisted of highly rated municipal auction rate securities. Auction rate securities provide liquidity via a Dutch auction process that resets the applicable interest rate at predetermined calendar intervals, usually every 28 days. This mechanism allows existing investors either to rollover their holdings, whereby they would continue to own their respective interest in the auction rate security, or to gain immediate liquidity by selling such interests at par. As of December 31, 2007, our investment portfolio included \$23.2 million of AAA/Aaa rated auction rate securities consisting of government-supported municipal debt obligations. None of the auction rate securities in our portfolio are mortgage-backed, and, through December 31, 2007, there had been no failed auctions related to these securities. In January 2008, our auction rate securities with January auction reset dates had successful auctions at which their interest rates were reset. In February 2008, we liquidated \$3.2 million of our auction rate securities at par, which were classified as short-term investments as of December 31, 2007. As of March 4, 2008, \$20.0 million of auction rate securities remained in our portfolio and auctions for these securities failed in February and early March 2008. As a result of this development and the remaining uncertainty in the market for auction rate securities, we have classified \$20.0 million of auction rate securities as long-term in the accompanying balance sheet as of December 31, 2007. These failures resulted in the interest rates on these investments resetting to contractually stipulated fail rates that are variable based on short-term municipal bond or other market indices, or fixed rates that may result in us earning above-market interest rates on these investments. If we need to access these funds, we will not be able to do so until a future auction on these investments is successful, the issuer redeems the outstanding securities, the securities mature, or we sell the securities in the secondary market.

In August 2007, we secured a new line of credit with General Electric Capital Corporation, or GE Capital, of up to \$3.0 million to finance certain equipment until September 30, 2008. The line of credit is subject to the terms of a Master Security Agreement, or MSA, between the Company and GE Capital, dated February 2001 and as amended on March 24, 2005 and related term sheet. As of December 31, 2007, we had not borrowed any funds under this line.





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As of December 31, 2007, future minimum payments under lease obligations and equipment financing lines were as follows (in thousands):

|                          | <b>Within<br/>One Year</b> | <b>Two to<br/>Three<br/>Years</b> | <b>Four to<br/>Five<br/>Years</b> | <b>After<br/>Five<br/>Years</b> | <b>Total</b>     |
|--------------------------|----------------------------|-----------------------------------|-----------------------------------|---------------------------------|------------------|
| Operating leases         | \$ 3,256                   | \$ 6,498                          | \$ 4,811                          | \$ 1,329                        | \$ 15,894        |
| Equipment financing line | 4,050                      | 3,654                             | 985                               |                                 | 8,689            |
| <b>Total</b>             | <b>\$ 7,306</b>            | <b>\$ 10,152</b>                  | <b>\$ 5,796</b>                   | <b>\$ 1,329</b>                 | <b>\$ 24,583</b> |

Our long-term commitments under operating leases relate to payments under our two facility leases in South San Francisco, California, which expire in 2011 and 2013.

Under the provisions of our amended agreement with Portola Pharmaceuticals, Inc., or Portola, we were obligated to reimburse Portola for certain equipment costs incurred by Portola in connection with research and related services that Portola provides to us. We began to incur these costs when the equipment became available for use in the second quarter of 2006. Our payments to Portola for such equipment costs, totaling \$285,000, were made in eight quarterly installments commencing in the first quarter of 2006 and through the fourth quarter of 2007. No further payments are due under this agreement.

In future periods, we expect to incur substantial costs as we continue to expand our research programs and related research and development activities. We also plan to continue to conduct clinical development of our cardiac myosin activator CK-1827452 for the potential treatment of heart failure, of ispinesib for the potential treatment of breast cancer and of SB-743921 for the potential treatment of Hodgkin and non-Hodgkin lymphoma. We expect to incur significant research and development expenses as we advance the research and development of our other cardiac myosin activators for the treatment of heart failure, pursue our other early stage research programs in multiple therapeutic areas and continue to refine and apply our existing and future proprietary drug discovery technologies.

Our future capital uses and requirements depend on numerous forward-looking factors. These factors include, but are not limited to, the following:

- the initiation, progress, timing, scope and completion of preclinical research, development and clinical trials for our drug candidates and potential drug candidates;

- the time and costs involved in obtaining regulatory approvals;

- delays that may be caused by requirements of regulatory agencies;

- if Amgen exercises its option, Amgen's decisions with regard to funding of development and commercialization of CK-1827452 or other compounds for the treatment of heart failure under our collaboration;

- GSK's decisions with regard to future funding of development of our drug candidates and potential drug candidates, including GSK-923295 and, if GSK exercises its option, either or both of ispinesib and SB-743921;

- our level of funding for the development of current or future drug candidates;

the number of drug candidates we pursue;

the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims;

our ability to establish, enforce and maintain selected strategic alliances and activities required for commercialization of our potential drugs;

our plans or ability to establish sales, marketing or manufacturing capabilities and to achieve market acceptance for potential drugs;

expanding and advancing our research programs;

hiring of additional employees and consultants;

expanding our facilities;

the acquisition of technologies, products and other business opportunities that require financial commitments; and

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our revenues, if any, from successful development of our drug candidates and commercialization of potential drugs.

We believe that our existing cash and cash equivalents, short- and long-term investments, interest earned on investments, proceeds from equipment financings and the potential proceeds from the 2007 CEFF will be sufficient to meet our projected operating requirements for at least the next 12 months. If, at any time, our prospects for internally financing our research and development programs decline, we may decide to reduce research and development expenses by delaying, discontinuing or reducing our funding of development of one or more of our drug candidates or potential drug candidates. Alternatively, we might raise funds through public or private financings, strategic relationships or other arrangements. There can be no assurance that the funding, if needed, will be available on attractive terms, or at all. Furthermore, any additional equity financing may be dilutive to stockholders and debt financing, if available, may involve restrictive covenants. Similarly, financing obtained through future co-development arrangements may require us to forego certain commercial rights to future drug candidates. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategy.

## **Off-balance Sheet Arrangements**

As of December 31, 2007, we did not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. In addition, we do not engage in trading activities involving non-exchange traded contracts. Therefore, we are not materially exposed to financing, liquidity, market or credit risk that could arise if we had engaged in these relationships. We do not have relationships or transactions with persons or entities that derive benefits from their non-independent relationship with us or our related parties.

## **Critical Accounting Policies and Estimates**

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and related disclosure of contingent assets and liabilities. We review our estimates on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our financial statements included in this Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

## ***Investments***

We invest in U.S. corporate, municipal and government agency bonds, commercial paper and certificates of deposit. The maturities of the investments range from three months to one year, with the exception of variable rate obligations as discussed below.

We have classified our investments as available-for-sale and, accordingly record them at fair value, based on quoted market rates, with unrealized gains and losses reflected as a separate component of stockholders' equity titled accumulated other comprehensive income (loss), net of tax, until realized or until a determination is made that an other-than-temporary decline in market value has occurred. Factors considered by management in assessing whether

an other-than-temporary impairment has occurred include: the nature of the investment; whether the decline in fair value is attributable to specific adverse conditions affecting the investment; the financial condition of the investee; the severity and the duration of the impairment; and whether we have the ability to hold the investment to maturity. When we determine that an other-than-temporary impairment has occurred, the investment is written down to its market value at the end of the period in which we determine that an other-than-temporary decline has occurred. The cost of marketable securities sold is based upon the specific identification method. We determined that no impairment of our investments existed at December 31, 2007. In addition, we classify investments as short-term or long-term based upon whether such assets are reasonably expected to be realized in cash or sold or consumed during the normal operating cycle of the business.

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The balance of our investments in auction rate securities was \$23.2 million at December 31, 2007 and \$29.9 million at December 31, 2006. Due to the resetting variable rates of these securities, their fair value generally approximates cost. There were no realized gains or losses from these investments during the years ended December 31, 2007, 2006 or 2005 and no cumulative unrealized gain or loss at December 31, 2007 or 2006. We recorded all income generated from these investments as interest income. There had been no failed auctions on any of our auction rate securities through December 31, 2007 and we deemed that no impairment existed as of that date. At December 31, 2007, we classified \$20.0 million of our investment in auction rate securities as long-term due to the uncertainty as to whether such securities will be available for current operations. See note 3 for additional details on our investment portfolio and events occurring subsequent to December 31, 2007 that impacted the classification of auction rate securities in our balance sheet.

All other available-for-sale investments are classified as short- or long-term investments according to their contractual maturities.

### ***Revenue Recognition***

We recognize revenue in accordance with Securities and Exchange Commission, or SEC, Staff Accounting Bulletin, or SAB, No. 104, Revenue Recognition. SAB No. 104 requires that basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured. Determination of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fee charged for research performed and milestones met, and the collectability of those fees. Should changes in conditions cause management to determine these criteria are not met for certain future transactions, revenue recognized for any reporting period could be adversely affected.

Research and development revenues, which are earned under agreements with third parties for contract research and development activities, may include nonrefundable license fees, research and development funding, cost reimbursements and contingent milestones and royalties. Our revenue arrangements with multiple elements are evaluated under Emerging Issues Task Force, or EITF, Issue No. 00-21, Revenue Arrangements with Multiple Deliverables, and are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer and whether there is objective and reliable evidence of the fair value of the undelivered items. The consideration we receive is allocated among the separate units based on their respective fair values, and the applicable revenue recognition criteria are applied to each of the separate units. Nonrefundable license fees are recognized as revenue as we perform under the applicable agreement. Where the level of effort is relatively consistent over the performance period, we recognize total fixed or determined revenue on a straight-line basis over the estimated period of expected performance.

We recognize milestone payments as revenue upon achievement of the milestone, provided the milestone payment is nonrefundable, substantive effort and risk is involved in achieving the milestone and the amount of the milestone is reasonable in relation to the effort expended or risk associated with the achievement of the milestone. If these conditions are not met, we defer the milestone payment and recognize it as revenue over the estimated period of performance under the contract as we complete our performance obligations.

Research and development revenues and cost reimbursements are based upon negotiated rates for our FTEs and actual out-of-pocket costs. FTE rates are intended to approximate our anticipated costs. Any amounts received in advance of performance are recorded as deferred revenue. None of the revenues recognized to date are refundable if the relevant research effort is not successful. In revenue arrangements in which both parties make payments to each other, we evaluate the payments in accordance with the provisions of EITF Issue No. 01-9, Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor's Products) to determine whether payments made by us

will be recognized as a reduction of revenue or as expense. In accordance with EITF Issue No. 01-9, revenue we recognize may be reduced by payments made to the other party under the arrangement unless we receive a separate and identifiable benefit in exchange for the payments and we can reasonably estimate the fair value of the benefit received. The application of EITF Issue No. 01-9 has had no impact to us.

Grant revenues are recorded as research is performed and are not refundable.

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***Preclinical Study and Clinical Trial Accruals***

A substantial portion of our preclinical studies and all of our clinical trials have been performed by third-party contract research organizations, or CROs, and other vendors. For preclinical studies, the significant factors used in estimating accruals include the percentage of work completed to date and contract milestones achieved. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, duration of enrollment and percentage of work completed to date. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence and status meetings with CROs and review of contractual terms. Our estimates are dependent on the timeliness and accuracy of data provided by our CROs and other vendors. If we have incomplete or inaccurate data, we may under- or overestimate activity levels associated with various studies or clinical trials at a given point in time. In this event, we could record adjustments to research and development expenses in future periods when the actual activity levels become known. No material adjustments to preclinical study and clinical trial expenses have been recognized to date.

***Stock-Based Compensation***

Effective January 1, 2006, we adopted the provisions of SFAS 123R, which establishes accounting for share-based payment awards made to employees and directors including employee stock options and employee stock purchases. Under No. 123R, stock-based compensation cost is measured at the grant date based on the calculated fair value of the award, and is recognized as an expense on a straight-line basis over the employee's requisite service period, generally the vesting period of the award. We elected the modified prospective transition method for awards granted subsequent to April 29, 2004, the date of our initial public offering, and the prospective transition method for awards granted prior to our initial public offering. Prior periods are not revised for comparative purposes under either transition method. Prior to January 1, 2006, we accounted for stock-based compensation to employees in accordance with Accounting Principles Board Opinion No. 25 and related interpretations. We also followed the disclosure requirements of SFAS No. 123, Accounting for Stock-Based Compensation, and complied with the disclosure requirements of SFAS No. 148, Accounting for Stock-Based Compensation Transition and Disclosure: an Amendment of FASB Statement No. 123.

We account for equity instruments issued to non-employees in accordance with the provisions of SFAS No. 123R and EITF Issue No. 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods, or Services.

As required under the accounting rules, we review our valuation assumptions at each grant date and, as a result, from time to time we will likely change the valuation assumptions we use to value stock based awards granted in future periods. The assumptions used in calculating the fair value of share-based payment awards represent management's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation expense could be materially different in the future. In addition, we are required to estimate the expected forfeiture rate and recognize expense only for those shares expected to vest. If our actual forfeiture rate is materially different from our estimate, the stock-based compensation expense could be significantly different from what we have recorded in the current period.

***Income taxes***

We record the estimated future tax effects of temporary differences between the tax bases of assets and liabilities and amounts reported in the financial statements, as well as operating loss and tax credit carry forwards. We have recorded a full valuation allowance to reduce our deferred tax asset to zero, because we believe that, based upon a number of factors, it is more likely than not that the deferred tax asset will not be realized. If we were to determine that we would be able to realize our deferred tax assets in the future, an adjustment to the deferred tax asset would increase net



income in the period such determination was made.

In July 2006, the FASB issued FIN 48. FIN 48 prescribes a comprehensive model for how companies should recognize, measure, present, and disclose in their financial statements uncertain tax positions taken or expected to be taken on a tax return. Under FIN 48, tax positions must initially be recognized in the financial statements when it is more likely than not the position will be sustained upon examination by the tax authorities. Such tax positions must initially and subsequently be measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon ultimate settlement with the tax authority assuming full knowledge of the position and relevant

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facts. We adopted FIN 48 on January 1, 2007. The cumulative effect of adopting FIN 48 was recorded net in deferred tax assets, which resulted in no FIN 48 liability on the balance sheet. The total amount of unrecognized tax benefits as of the date of adoption was \$3.1 million. See Notes to Condensed Consolidated Financial Statements, Note 11 Income Taxes for additional information. As of December 31, 2007, our unrecognized tax benefits were \$3.5 million.

## **Recent Accounting Pronouncements**

In September 2006, the FASB issued SFAS No. 157, Fair Value Measurements, or SFAS No. 157. This standard defines fair value, establishes a framework for measuring fair value in accounting principles generally accepted in the United States of America, and expands disclosure about fair value measurements. This pronouncement applies under the other accounting standards that require or permit fair value measurements. Accordingly, this statement does not require any new fair value measurement. SFAS No. 157 is effective for fiscal years beginning after November 15, 2007 and interim periods within those fiscal years, for all financial assets and liabilities and for nonfinancial assets and liabilities that are recognized or disclosed at fair value at least annually. It is effective for fiscal years beginning after November 15, 2008 for all other nonfinancial assets and liabilities. SFAS No. 157 is to be applied prospectively. We do not expect that the adoption of the requirements of SFAS 157 that are effective on January 1, 2008 will have a material impact on our financial position or results of operations. We are currently evaluating the requirements of SFAS No. 157 that will become effective for it on January 1, 2009, and have not yet determined the impact, if any, on the financial statements.

In February 2007, the FASB issued SFAS No. 159, The Fair Value Option for Financial Assets and Financial Liabilities, or SFAS 159, which permits entities to choose to measure many financial instruments and certain other items at fair value that are not currently required to be measured at fair value. SFAS No. 159 is effective for us on January 1, 2008. We do not expect that the adoption of SFAS No. 159 will have a material impact on our financial position or results of operations.

In June 2007, the EITF reached a consensus on EITF Issue No. 07-3, Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities. EITF Issue No. 07-3 states that nonrefundable advance payments for future research and development activities should be deferred and recognized as an expense as the goods are delivered or the related services are performed. Entities should then continue to evaluate whether they expect the goods to be delivered or services to be rendered. If an entity does not expect the goods to be delivered or services to be rendered, the capitalized advance payment should be charged to expense. EITF Issue No. 07-3 will be effective for us on January 1, 2008 and is to be applied prospectively for new contracts entered into on or after the effective date. We are currently evaluating the impact on our financial statements of adopting EITF Issue No. 07-3.

In November 2007, the EITF issued a consensus on EITF Issue No. 07-01, Accounting for Collaboration Arrangements Related to the Development and Commercialization of Intellectual Property, which is focused on how the parties to a collaborative agreement should account for costs incurred and revenue generated on sales to third parties, how shared payments pursuant to a collaboration agreement should be presented in the income statement and certain related disclosure questions. EITF Issue No. 07-01 is to be applied retrospectively for collaboration arrangements in fiscal years beginning after December 15, 2008. We are currently evaluating the impact on its financial statements of adopting EITF Issue No. 07-1.

In December 2007, the SEC issued SAB No. 110, which addresses the continued use of the simplified method for estimating the expected term for stock-based compensation. Previously, under SAB No. 107, Share-Based Payment, the use of the simplified method was intended to be discontinued after December 31, 2007. Under SAB No. 110, companies may continue to use the simplified method in certain circumstances. We have used the simplified method of estimating the expected term for stock-based compensation since its adoption of SFAS No. 123R on January 1,

2006, and are in the process of determining the effect, if any, the adoption of SAB No. 110 on our financial statements.

**Table of Contents****ITEM 7A. Quantitative and Qualitative Disclosures About Market Risks****Interest Rate Sensitivity**

Our exposure to market risk is limited to interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term debt securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. We are exposed to the impact of interest rate changes and changes in the market values of our investments. Our interest income is sensitive to changes in the general level of U.S. interest rates. Our exposure to market rate risk for changes in interest rates relates primarily to our investment portfolio. We have not used derivative financial instruments in our investment portfolio. We invest a portion of our excess cash in debt instruments of high-quality issuers and, by policy, limit the amount of credit exposure in any one issuer and investment class. We protect and preserve our invested funds by limiting default, market and reinvestment risk. Investments in both fixed-rate and floating-rate interest-earning instruments carry a degree of interest rate risk. Fixed-rate securities may have their fair market value adversely impacted due to a rise in interest rates, while floating-rate securities may produce less income than expected if interest rates fall. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates.

To minimize risk, we maintain our portfolio of cash and cash equivalents and short- and long-term investments in a variety of interest-bearing instruments, including U.S. government and agency securities, high grade municipal and U.S. corporate bonds, commercial paper, certificates of deposit and money market funds. Our investment portfolio of short-term investments is subject to interest rate risk, and will fall in value if market interest rates increase. As of December 31, 2007, our investments consist of highly rated municipal auction rate securities. Auction rate securities provide liquidity via a Dutch auction process that resets the applicable interest rate at predetermined calendar intervals, or auction reset dates, usually every 28 days. This mechanism allows existing investors either to roll over their holdings, whereby they would continue to own their respective interest in the auction rate security, or to gain immediate liquidity by selling such interests at par. See further discussion of our investment securities portfolio and auction rate securities holdings in the Liquidity and Capital Resources section of Item 7 of this Form 10-K.

Our cash and cash equivalents are invested in highly liquid securities with original maturities of three months or less at the time of purchase; consequently, we do not consider our cash and cash equivalents to be subject to significant interest rate risk and have therefore excluded them from the table below. On the liability side, our equipment financing lines carry fixed interest rates and therefore also may be subject to changes in fair value if market interest rates fluctuate. We do not have any foreign currency or derivative financial instruments.

The table below presents the principal amounts and weighted average interest rates by year of maturity for our investment portfolio and equipment financing lines (dollars in thousands):

|                          | 2008  | 2009 | 2010 | 2011 | 2012 | Beyond<br>2012 | Total     | Fair<br>Value at<br>December 31,<br>2007 |
|--------------------------|-------|------|------|------|------|----------------|-----------|--|
| <b>Assets:</b>           |       |      |      |      |      |                |           |  |
| Investments              | 3,175 |      |      |      |      | \$ 20,025      | \$ 23,200 | \$ 23,200                                |
| Average<br>interest rate | 6.45% |      |      |      |      | 6.28%          | 6.31%     |  |

**Liabilities:**

|                           |          |          |          |        |        |  |          |          |
|---------------------------|----------|----------|----------|--------|--------|--|----------|----------|
| Equipment financing lines | \$ 4,050 | \$ 2,025 | \$ 1,629 | \$ 833 | \$ 152 |  | \$ 8,689 | \$ 8,502 |
| Average interest rate     | 5.27%    | 6.39%    | 6.82%    | 7.31%  | 7.25%  |  | 6.05%    |          |

**ITEM 8. *Financial Statements and Supplementary Data***

**CYTOKINETICS, INCORPORATED  
(A Development Stage Enterprise)  
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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Stockholders of Cytokinetics, Incorporated:

In our opinion, the accompanying balance sheets and the related statement of operations, stockholders' equity (deficit) and cash flows present fairly, in all material respects, the financial position of Cytokinetics, Incorporated (a development stage company) at December 31, 2007 and 2006, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2007 and cumulatively, for the period from August 5, 1997 (date of inception) to December 31, 2007 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2007, based on criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

As discussed in Note 1 to the financial statements, the Company changed the manner in which it accounts for stock-based compensation in 2006.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PRICEWATERHOUSECOOPERS LLP  
San Jose, CA  
March 11, 2008



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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**BALANCE SHEETS**

|   | <b>December 31,</b>                                    |                |
|---|--|----------------|
|   | <b>2007</b>  | <b>2006</b>    |
|   | <b>(In thousands, except share and per share data)</b> |                |
| <b>ASSETS</b>   |  |                |
| Current assets:   |  |                |
| Cash and cash equivalents   | \$ 116,564   | \$ 39,387      |
| Short-term investments  | 3,175  | 70,155         |
| Related party accounts receivable   | 87   | 42,071         |
| Related party notes receivable - short-term portion                             | 127  | 160            |
| Prepaid and other current assets  | 2,063  | 1,848          |
| <br>Total current assets  | <br>122,016  | <br>153,621    |
| Long-term investments   | 20,025   |                |
| Property and equipment, net   | 7,728  | 9,202          |
| Related party notes receivable - long-term portion                              | 99   | 292            |
| Restricted cash   | 5,167  | 6,034          |
| Other assets  | 335  | 367            |
| <br>Total assets  | <br>\$ 155,370   | <br>\$ 169,516 |
| <b>LIABILITIES AND STOCKHOLDERS EQUITY</b>                                      |  |                |
| Current liabilities:  |  |                |
| Accounts payable  | \$ 1,584   | \$ 2,838       |
| Accrued liabilities   | 8,558  | 7,466          |
| Related party payables and accrued liabilities                                  | 22   | 164            |
| Short-term portion of equipment financing lines                                 | 4,050  | 3,691          |
| Short-term portion of deferred revenue  | 12,234   | 12,234         |
| <br>Total current liabilities   | <br>26,448   | <br>26,393     |
| Long-term portion of equipment financing lines                                  | 4,639  | 7,144          |
| Long-term portion of deferred revenue   | 24,367   | 29,666         |
| <br>Total liabilities   | <br>55,454   | <br>63,203     |
| <br>Commitments and contingencies (Note 8)                                      |  |                |
| Stockholders' equity:   |  |                |
| Common stock, \$0.001 par value:  |  |                |
| Authorized: 120,000,000 shares  |  |                |
| Issued and outstanding: 49,282,362 shares in 2007 and 43,283,558 shares in 2006 | 49   | 43             |
| Additional paid-in capital  | 379,730  | 338,078        |

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|  |            |            |
|--|------------|------------|
| Deferred stock-based compensation                | (329)      | (1,094)    |
| Accumulated other comprehensive loss             | (1)        | (75)       |
| Deficit accumulated during the development stage | (279,533)  | (230,639)  |
| Total stockholders' equity                       | 99,916     | 106,313    |
| Total liabilities and stockholders' equity       | \$ 155,370 | \$ 169,516 |

The accompanying notes are an integral part of these financial statements.

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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**STATEMENTS OF OPERATIONS**

|   | <b>Years Ended December 31,</b>              |                    |                    | <b>Period from</b>   |
|---|--|--------------------|--------------------|----------------------|
|   | <b>2007</b>                                  | <b>2006</b>        | <b>2005</b>        | <b>August 5,</b>     |
|   |  |                    |                    | <b>1997</b>          |
|   |  |                    |                    | <b>(Date of</b>      |
|   |  |                    |                    | <b>Inception) to</b> |
|   |  |                    |                    | <b>December 31,</b>  |
|   |  |                    |                    | <b>2007</b>          |
|   | <b>(In thousands, except per share data)</b> |                    |                    |                      |
| Revenues:   |  |                    |                    |                      |
| Research and development revenues from related party  | \$ 1,388                                     | \$ 1,622           | \$ 4,978           | \$ 40,253            |
| Research and development, grant and other revenues  |  | 4                  | 1,134              | 2,955                |
| License revenues from related parties   | 12,234                                       | 1,501              | 2,800              | 26,335               |
| <b>Total revenues</b>   | <b>13,622</b>                                | <b>3,127</b>       | <b>8,912</b>       | <b>69,543</b>        |
| Operating expenses:   |  |                    |                    |                      |
| Research and development(1)   | 53,388                                       | 49,225             | 40,570             | 283,488              |
| General and administrative(1)   | 16,721                                       | 15,240             | 12,975             | 85,461               |
| <b>Total operating expenses</b>   | <b>70,109</b>                                | <b>64,465</b>      | <b>53,545</b>      | <b>368,949</b>       |
| Operating loss  | (56,487)                                     | (61,338)           | (44,633)           | (299,406)            |
| Interest and other income   | 8,292  | 4,746              | 2,916              | 24,743               |
| Interest and other expense  | (699)  | (523)              | (535)              | (4,870)              |
| <b>Net loss</b>   | <b>\$ (48,894)</b>                           | <b>\$ (57,115)</b> | <b>\$ (42,252)</b> | <b>\$ (279,533)</b>  |
| Net loss per common share basic and diluted   | \$ (1.03)                                    | \$ (1.56)          | \$ (1.48)          |                      |
| Weighted-average number of shares used in computing net loss per common share basic and diluted |  |                    |                    |                      |
|   | 47,590                                       | 36,618             | 28,582             |                      |
| (1) Includes the following stock-based compensation charges:                                    |  |                    |                    |                      |
| Research and development  | \$ 2,932                                     | \$ 2,532           | \$ 790             | \$ 8,312             |
| General and administrative  | 2,621  | 2,111              | 637                | 6,435                |

The accompanying notes are an integral part of these financial statements.



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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT)**

|  | Common Stock                                    | Additional Paid-In Capital |         | Deferred Stock-Based Compensation | Accumulated Other Comprehensive Income (Loss) | Deficit Accumulated During the Development Stage | Total Stockholders Equity (Deficit) |
|--|---|----------------------------|---------|-----------------------------------|---|--|-------------------------------------|
|  | Shares  | Amount                     | Capital | Compensation                      | (Loss)  | Stage  | (Deficit)                           |
|  | (In thousands, except share and per share data) |                            |         |                                   |   |  |                                     |
| Issuance of common stock upon exercise of stock options for cash at \$0.015 per share          | 147,625   | \$                         | \$ 2    |                                   | \$  | \$   | \$ 2                                |
| Issuance of common stock to founders at \$0.015 per share in exchange for cash in January 1998 | 563,054   | 1                          | 7       |                                   |   |  | 8                                   |
| Net loss   |   |                            |         |                                   |   | (2,015)  | (2,015)                             |
| Balances, December 31, 1998  | 710,679   | 1                          | 9       |                                   |   | (2,015)  | (2,005)                             |
| Issuance of common stock upon exercise of stock options for cash at \$0.015-\$0.58 per share   | 287,500   |                            | 69      |                                   |   |  | 69                                  |
| Issuance of warrants, valued using Black-Scholes model   |   |                            | 41      |                                   |   |  | 41                                  |
| Deferred stock-based compensation  |   |                            | 237     | (237)                             |   |  |                                     |
| Amortization of deferred stock-based compensation  |   |                            |         | 123                               |   |  | 123                                 |
| Components of comprehensive loss:  |   |                            |         |                                   |   |  |                                     |
| Change in unrealized gain (loss) on investments  |   |                            |         |                                   | (8)   |  | (8)                                 |
| Net loss   |   |                            |         |                                   |   | (7,341)  | (7,341)                             |
| Total comprehensive loss   |   |                            |         |                                   |   |  | (7,349)                             |

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|  |           |      |        |         |        |             |             |
|--|-----------|------|--------|---------|--------|-------------|-------------|
| Balances, December 31, 1999  | 998,179   | 1    | 356    | (114)   | (8)    | (9,356)     | (9,121)     |
| Issuance of common stock upon exercise of stock options for cash at \$0.015-\$0.58 per share | 731,661   | 1    | 194    |         |        |             | 195         |
| Deferred stock-based compensation  |           |      | 93     | (93)    |        |             |             |
| Amortization of deferred stock-based compensation  |           |      |        | 101     |        |             | 101         |
| Components of comprehensive loss:  |           |      |        |         |        |             |             |
| Change in unrealized gain (loss) on investments  |           |      |        |         | 86     |             | 86          |
| Net loss   |           |      |        |         |        | (13,079)    | (13,079)    |
| Total comprehensive loss   |           |      |        |         |        |             | (12,993)    |
| Balances, December 31, 2000  | 1,729,840 | 2    | 643    | (106)   | 78     | (22,435)    | (21,818)    |
| Issuance of common stock upon exercise of stock options for cash at \$0.015-\$1.20 per share | 102,480   |      | 56     |         |        |             | 56          |
| Repurchase of common stock   | (33,334)  |      | (19)   |         |        |             | (19)        |
| Compensation expense for acceleration of options   |           |      | 20     |         |        |             | 20          |
| Deferred stock-based compensation  |           |      | 45     | (45)    |        |             |             |
| Amortization of deferred stock-based compensation  |           |      |        | 93      |        |             | 93          |
| Components of comprehensive loss:  |           |      |        |         |        |             |             |
| Change in unrealized gain (loss) on investments  |           |      |        |         | 190    |             | 190         |
| Net loss   |           |      |        |         |        | (15,874)    | (15,874)    |
| Total comprehensive loss   |           |      |        |         |        |             | (15,684)    |
| Balances, December 31, 2001  | 1,798,986 | \$ 2 | \$ 745 | \$ (58) | \$ 268 | \$ (38,309) | \$ (37,352) |
| Issuance of common stock upon exercise of  | 131,189   | \$   | \$ 68  | \$      | \$     | \$          | \$ 68       |

|   |         |     |          |          |
|---|---------|-----|----------|----------|
| stock options for cash at<br>\$0.015-\$1.20 per share |         |     |          |          |
| Repurchase of common<br>stock                         | (3,579) | (2) |          | (2)      |
| Deferred stock-based<br>compensation                  |         | (2) | 2        |          |
| Amortization of<br>deferred compensation              |         |     | 6        | 6        |
| Components of<br>comprehensive loss:                  |         |     |          |          |
| Change in unrealized<br>gain (loss) on<br>investments |         |     | (228)    | (228)    |
| Net loss  |         |     | (23,080) | (23,080) |
| Total comprehensive<br>loss                           |         |     |          | (23,308) |

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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT) (Continued)**

|  | <b>Common Stock</b>                                    |               | <b>Additional</b> | <b>Deferred</b>     | <b>Other</b>        | <b>Accumulated</b> | <b>Total</b>        |
|--|--|---------------|-------------------|---------------------|---------------------|--------------------|---------------------|
|  | <b>Shares</b>  | <b>Amount</b> | <b>Paid-In</b>    | <b>Stock-Based</b>  | <b>Comprehensiv</b> | <b>During the</b>  | <b>Stockholders</b> |
|  |  |               | <b>Capital</b>    | <b>Compensation</b> | <b>Income</b>       | <b>Development</b> | <b>Equity</b>       |
|  |  |               |                   | <b>(Loss)</b>       |                     | <b>Stage</b>       | <b>(Deficit)</b>    |
|  | <b>(In thousands, except share and per share data)</b> |               |                   |                     |                     |                    |                     |
| Balances, December 31, 2002  | 1,926,596  | 2             | 809               | (50)                | 40                  | (61,389)           | (60,588)            |
| Issuance of common stock upon exercise of stock options for cash at \$0.20-\$1.20 per share                  | 380,662  |               | 310               |                     |                     |                    | 310                 |
| Stock-based compensation   |  |               | 158               |                     |                     |                    | 158                 |
| Deferred stock-based compensation  |  |               | 4,369             | (4,369)             |                     |                    |                     |
| Amortization of deferred stock-based compensation  |  |               |                   | 768                 |                     |                    | 768                 |
| Components of comprehensive loss:  |  |               |                   |                     |                     |                    |                     |
| Change in unrealized gain (loss) on investments  |  |               |                   |                     | 6                   |                    | 6                   |
| Net loss   |  |               |                   |                     |                     | (32,685)           | (32,685)            |
| Total comprehensive loss   |  |               |                   |                     |                     |                    | (32,679)            |
| Balances, December 31, 2003  | 2,307,258  | 2             | 5,646             | (3,651)             | 46                  | (94,074)           | (92,031)            |
| Issuance of common stock upon initial public offering at \$13.00 per share, net of issuance costs of \$9,151 | 7,935,000  | 8             | 93,996            |                     |                     |                    | 94,004              |
| Issuance of common stock to related party for \$13.00 per share  | 538,461  | 1             | 6,999             |                     |                     |                    | 7,000               |
| Issuance of common stock to related party  | 37,482   |               |                   |                     |                     |                    |                     |
| Conversion of preferred stock to common stock upon initial public offering                                   | 17,062,145   | 17            | 133,155           |                     |                     |                    | 133,172             |
|  | 115,358  |               |                   |                     |                     |                    |                     |



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|  |            |       |            |            |          |              |    |          |
|--|------------|-------|------------|------------|----------|--------------|----|----------|
| Issuance of common stock upon cashless exercise of warrants  |            |       |            |            |          |              |    |          |
| Issuance of common stock upon exercise of stock options for cash at \$0.20-\$6.50 per share  | 404,618    |       | 430        |            |          |              |    | 430      |
| Issuance of common stock pursuant to ESPP at \$8.03 per share  | 69,399     |       | 557        |            |          |              |    | 557      |
| Stock-based compensation   |            |       | 278        |            |          |              |    | 278      |
| Deferred stock-based compensation  |            |       | 2,198      | (2,198)    |          |              |    |          |
| Amortization of deferred stock-based compensation  |            |       |            | 1,598      |          |              |    | 1,598    |
| Repurchase of unvested stock   | (16,548)   |       | (20)       |            |          |              |    | (20)     |
| Components of comprehensive loss:  |            |       |            |            |          |              |    |          |
| Change in unrealized gain (loss) on investments  |            |       |            |            | (234)    |              |    | (234)    |
| Net loss   |            |       |            |            |          | (37,198)     |    | (37,198) |
| Total comprehensive loss   |            |       |            |            |          |              |    | (37,432) |
| Balances, December 31, 2004  | 28,453,173 | \$ 28 | \$ 243,239 | \$ (4,251) | \$ (188) | \$ (131,272) | \$ | 107,556  |
| Issuance of common stock upon exercise of stock options for cash at \$0.58-\$7.10 per share  | 196,703    | \$ 1  | \$ 370     | \$         | \$       | \$           | \$ | 371      |
| Issuance of common stock pursuant to ESPP at \$4.43 per share  | 179,520    |       | 763        |            |          |              |    | 763      |
| Issuance of common stock upon cashless exercise of warrants  | 14,532     |       |            |            |          |              |    |          |
| Issuance of common stock upon drawdown of committed equity financing facility at \$6.13-\$7.35 per share, net of issuance costs of \$178 | 887,576    | 1     | 5,546      |            |          |              |    | 5,547    |
| Stock-based compensation   |            |       | 67         |            |          | 67           |    |          |
| Amortization of deferred stock-based compensation, net of cancellations  |            |       | (439)      | 1,799      |          |              |    | 1,360    |
| Repurchase of unvested stock   | (20,609)   |       | (25)       |            |          |              |    | (25)     |
| Components of comprehensive loss:  |            |       |            |            |          |              |    |          |

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|  |     |          |          |
|--|-----|----------|----------|
| Change in unrealized gain<br>(loss) on investments | 174 |          | 174      |
| Net loss   |     | (42,252) | (42,252) |
| Total comprehensive loss                           |     |          | (42,078) |

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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT) (Continued)**

|   | <b>Common Stock</b>                                    |               | <b>Additional Paid-In Capital</b> |                     | <b>Deferred Compensation</b>             |                                     | <b>Accumulated Deficit</b> |  | <b>Total Stockholders Equity (Deficit)</b> |          |
|---|--|---------------|-----------------------------------|---------------------|--|-------------------------------------|----------------------------|--|--|----------|
|   | <b>Shares</b>  | <b>Amount</b> | <b>Capital</b>                    | <b>Compensation</b> | <b>Other Comprehensive Income (Loss)</b> | <b>During the Development Stage</b> |                            |  |  |          |
|   | <b>(In thousands, except share and per share data)</b> |               |                                   |                     |  |                                     |                            |  |  |          |
| Balances, December 31, 2005   | 29,710,895   | 30            | 249,521                           | (2,452)             | (14)                                     | (173,524)                           |                            |  | 73,561                                     |          |
| Issuance of common stock upon exercise of stock options for cash at \$0.20-\$7.10 per share                                       | 354,502  |               | 559                               |                     |  |                                     |                            |  | 559  |          |
| Issuance of common stock pursuant to ESPP at a weighted price of \$4.43 per share   | 193,248  |               | 856                               |                     |  |                                     |                            |  | 856  |          |
| Issuance of common stock pursuant to registered direct offerings at \$6.60 and \$7.00 per share, net of issuance costs of \$3,083 | 10,285,715   | 10            | 66,907                            |                     |  |                                     |                            |  | 66,917                                     |          |
| Issuance of common stock upon drawdown of committed equity financing facility at \$5.53-\$7.02 per share                          | 2,740,735  | 3             | 16,954                            |                     |  |                                     |                            |  | 16,957                                     |          |
| Stock-based compensation  |  |               | 3,421                             |                     |  |                                     |                            |  | 3,421                                      |          |
| Amortization of deferred stock-based compensation, net of cancellations   |  |               | (138)                             | 1,358               |  |                                     |                            |  | 1,220                                      |          |
| Repurchase of unvested stock  | (1,537)  |               | (2)                               |                     |  |                                     |                            |  | (2)  |          |
| Components of comprehensive loss:   |  |               |                                   |                     |  |                                     |                            |  |  |          |
| Change in unrealized gain (loss) on investments   |  |               |                                   |                     | (61)                                     |                                     |                            |  | (61)                                       |          |
| Net loss  |  |               |                                   |                     |  | (57,115)                            |                            |  | (57,115)                                   |          |
| Total comprehensive loss  |  |               |                                   |                     |  |                                     |                            |  |  | (57,176) |

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|  |            |       |            |            |         |              |            |
|--|------------|-------|------------|------------|---------|--------------|------------|
| Balances, December 31, 2006  | 43,283,558 | \$ 43 | \$ 338,078 | \$ (1,094) | \$ (75) | \$ (230,639) | \$ 106,313 |
| Issuance of common stock upon exercise of stock options for cash at \$0.58-\$7.10 per share              | 259,054    | 1     | 511        |            |         |              | 512        |
| Issuance of common stock pursuant to ESPP at a weighted price of \$4.49 per share                        | 179,835    |       | 807        |            |         |              | 807        |
| Issuance of common stock upon drawdown of committed equity financing facility at \$4.43-\$4.81 per share | 2,075,177  | 2     | 9,540      |            |         |              | 9,542      |
| Issuance of common stock to related party for \$9.47 per share, net of issuance costs of \$57            | 3,484,806  | 3     | 26,006     |            |         |              | 26,009     |
| Stock-based compensation   |            |       | 4,833      |            |         |              | 4,833      |
| Amortization of deferred stock-based compensation, net of cancellations                                  |            |       | (45)       | 765        |         |              | 720        |
| Repurchase of unvested stock   | (68)       |       |            |            |         |              |            |
| Components of comprehensive loss:  |            |       |            |            |         |              |            |
| Change in unrealized gain (loss) on investments  |            |       |            |            | 74      |              | 74         |
| Net loss   |            |       |            |            |         | (48,894)     | (48,894)   |
| Total comprehensive loss   |            |       |            |            |         |              | (48,820)   |
| Balances, December 31, 2007  | 49,282,362 | \$ 49 | \$ 379,730 | \$ (329)   | \$ (1)  | \$ (279,533) | \$ 99,916  |

The accompanying notes are an integral part of these financial statements.

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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**STATEMENTS OF CASH FLOWS**

|  | Years Ended December 31, |             |             | Period from                                       |
|--|--------------------------|-------------|-------------|---|
|  | 2007                     | 2006        | 2005        | August 5,<br>1997                                 |
|  | (In thousands)           |             |             | (Date of<br>Inception) to<br>December 31,<br>2007 |
| <b>Cash flows from operating activities:</b>   |                          |             |             |   |
| Net loss   | \$ (48,894)              | \$ (57,115) | \$ (42,252) | \$ (279,533)                                      |
| Adjustments to reconcile net loss to net cash used in operating activities:                  |                          |             |             |   |
| Depreciation and amortization of property and equipment                                      | 2,829                    | 2,927       | 3,062       | 20,989  |
| (Gain) loss on disposal of equipment   | 13                       | (8)         | 25          | 348   |
| Gain on sale of investments  |                          |             |             | (84)  |
| Allowance for doubtful accounts  |                          |             |             | 191   |
| Non-cash expense related to warrants issued for equipment financing lines and facility lease |                          |             |             | 41  |
| Non-cash interest expense  | 92                       | 92          | 92          | 427   |
| Non-cash forgiveness of loan to officer  | 116                      | 107         | 60          | 364   |
| Stock-based compensation   | 5,553                    | 4,643       | 1,427       | 14,747  |
| Other non-cash expenses  | 7                        |             |             | 27  |
| Changes in operating assets and liabilities:   |                          |             |             |   |
| Accounts receivable  |                          |             |             |   |
| Related party accounts receivable  | 41,959                   | (41,515)    | (544)       | (427)   |
| Prepaid and other assets   | (275)                    | 413         | 565         | (2,350)   |
| Accounts payable   | (969)                    | 852         | (191)       | 1,394   |
| Accrued liabilities  | 2,005                    | 2,419       | 519         | 8,522   |
| Related party payables and accrued liabilities   | (142)                    | (485)       | 553         | 22  |
| Deferred revenue   | (5,299)                  | 40,500      | (2,800)     | 36,601  |
| Net cash used in operating activities  | (3,005)                  | (47,170)    | (39,484)    | (198,721)   |
| <b>Cash flows from investing activities:</b>   |                          |             |             |   |
| Purchases of investments   | (51,700)                 | (143,046)   | (89,326)    | (644,903)   |
| Proceeds from sales and maturities of investments  | 98,729                   | 135,527     | 123,995     | 621,786   |
| Purchases of property and equipment  | (2,563)                  | (5,370)     | (1,465)     | (28,892)  |
| Proceeds from sale of property and equipment   |                          | 6           | 20          | 50  |
| (Increase) decrease in restricted cash   | 867                      | (862)       | 808         | (5,167)   |
| Issuance of related party notes receivable   |                          |             |             | (1,146)   |
| Proceeds from repayments of notes receivable   | 129                      | 63          | 460         | 699   |

|  |            |           |           |            |
|--|------------|-----------|-----------|------------|
| Net cash provided by (used in) investing activities  | 45,462     | (13,682)  | 34,492    | (57,573)   |
| <b>Cash flows from financing activities:</b>   |            |           |           |            |
| Proceeds from initial public offering, sale of common stock to related party and public offerings, net of issuance costs | 26,012     | 66,917    |           | 193,934    |
| Proceeds from draw down of Committed Equity Financing Facility, net of issuance costs                                    | 9,542      | 16,957    | 5,547     | 32,046     |
| Proceeds from other issuances of common stock  | 1,312      | 1,378     | 1,054     | 5,558      |
| Proceeds from issuance of preferred stock, net of issuance costs   |            |           |           | 133,172    |
| Repurchase of common stock   |            | (2)       | (25)      | (68)       |
| Proceeds from equipment financing lines  | 1,742      | 4,347     | 1,280     | 23,696     |
| Repayment of equipment financing lines   | (3,888)    | (2,873)   | (2,410)   | (15,480)   |
| Net cash provided by financing activities  | 34,720     | 86,724    | 5,446     | 372,858    |
| Net increase in cash and cash equivalents  | 77,177     | 25,872    | 454       | 116,564    |
| Cash and cash equivalents, beginning of period   | 39,387     | 13,515    | 13,061    |            |
| Cash and cash equivalents, end of period   | \$ 116,564 | \$ 39,387 | \$ 13,515 | \$ 116,564 |

The accompanying notes are an integral part of these financial statements.

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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**NOTES TO FINANCIAL STATEMENTS**

**Note 1 Organization and Significant Accounting Policies**

***Organization***

Cytokinetics, Incorporated (the Company, we or our) was incorporated under the laws of the state of Delaware on August 5, 1997. The Company is focused on developing small molecule therapeutics for the treatment of cardiovascular diseases and cancer. The Company is a development stage enterprise and has been primarily engaged in conducting research, developing drug candidates and technologies, and raising capital.

The Company has funded its operations primarily through sales of common stock and convertible preferred stock, contract payments under its collaboration agreements, debt financing arrangements, government grants and interest income. On April 26, 2004 the Company effected a one for two reverse stock split. All share and per share amounts for all periods presented in the accompanying financial statements have been retroactively adjusted to give effect to the reverse stock split.

The Company's registration statement for its initial public offering (IPO) was declared effective by the Securities and Exchange Commission (SEC) on April 29, 2004. The Company's common stock commenced trading on the NASDAQ National Market, now the NASDAQ Global Market, on April 29, 2004 under the trading symbol CYTK.

Prior to achieving profitable operations, the Company intends to fund operations through the additional sale of equity securities, payments from strategic collaborations, government grant awards and debt financing.

***Use of Estimates***

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

***Concentration of Credit Risk and Other Risks and Uncertainties***

Financial instruments that potentially subject the Company to concentrations of risk consist principally of cash and cash equivalents, investments and accounts receivable. The Company's cash, cash equivalents and investments are invested in deposits with four major financial institutions in the United States. Deposits in these banks may exceed the amount of insurance provided on such deposits. The Company has not experienced any losses on its deposits of cash, cash equivalents or investments.

The Company performs an ongoing credit evaluation of its strategic partners' financial conditions and generally does not require collateral to secure accounts receivable from its strategic partners. The Company's exposure to credit risk associated with non-payment is affected principally by conditions or occurrences within Amgen Inc. (Amgen), and GlaxoSmithKline (GSK), its primary strategic partners. Approximately 90% of total revenues for the year ended December 31, 2007, and less than 10% for the year ended December 31, 2006 were derived from Amgen. The

Company earned no revenues from Amgen prior to 2006. Accounts receivable from Amgen was zero at December 31, 2007 and \$42.0 million at December 31, 2006 and was included in related party accounts receivable. Approximately 10% of revenues for the year ended December 31, 2007, 97% of revenues for the year ended December 31, 2006, and 87% of revenues for the year ended December 31, 2005 were derived from GSK. Accounts receivable from GSK totaled \$19,000 at December 31, 2007 and \$45,000 at December 31, 2006 and was included in related party accounts receivable. See also Note 5, Related Party Transactions, below regarding collaboration agreements with Amgen and GSK. Revenues from AstraZeneca AB ( AstraZeneca ) were none in each of the years ended December 31, 2007 and December 31, 2006, and 13% of total revenues in the year ended December 31, 2005.



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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

Drug candidates developed by the Company may require approvals or clearances from the U.S. Food and Drug Administration ( FDA ) or international regulatory agencies prior to commercialized sales. There can be no assurance that the Company s drug candidates will receive any of the required approvals or clearances. If the Company were to be denied approval or clearance or any such approval or clearance were to be delayed, it would have a material adverse impact on the Company.

The Company s operations and employees are located in the United States. In the years ended December 31, 2007, 2006 and 2005, all of the Company s revenues were received from entities located in the United States or from United States affiliates of foreign corporations.

***Cash and Cash Equivalents***

The Company considers all highly liquid investments with a maturity of three months or less at the time of purchase to be cash equivalents.

***Investments***

The Company invests in U.S. corporate, municipal and government agency bonds, commercial paper and certificates of deposit. The maturities of the investments range from three months to one year, with the exception of variable rate obligations as discussed below.

The Company has classified its investments as available-for-sale and, accordingly, records them at fair value, net of tax, based on quoted market rates. Unrealized gains and losses are reflected as a separate component of stockholders equity, Accumulated Other Comprehensive Income (Loss), until realized or until a determination is made that an other-than-temporary decline in market value has occurred. Factors considered by management in assessing whether an other-than-temporary impairment has occurred include: the nature of the investment; whether the decline in fair value is attributable to specific adverse conditions affecting the investment; the financial condition of the investee; the severity and the duration of the impairment; and whether the Company has the ability to hold the investment to maturity. When it is determined that an other-than-temporary impairment has occurred, the investment is written down to its market value at the end of the period in which it is determined that an other-than-temporary decline has occurred. The cost of marketable securities sold is based upon the specific identification method. The Company determined that no impairment of its investments existed at December 31, 2007. In addition, the Company classifies investments as short-term or long-term based upon whether such assets are reasonably expected to be realized in cash or sold or consumed during the normal operating cycle of the business.

The balance of the Company s short- and long-term investments in auction rate securities totaled \$23.2 million at December 31, 2007 and \$29.9 million at December 31, 2006. Due to the resetting variable rates of these securities, their fair value generally approximates cost. There were no realized gains or losses from these investments during the years ended December 31, 2007, 2006 or 2005 and no cumulative unrealized gain or loss at December 31, 2007 or 2006. All income generated from these investments was recorded as interest income. There had been no failed auctions on any of the Company s auction rate securities through December 31, 2007 and the Company deemed that no impairment existed as of that date. At December 31, 2007, the Company classified \$20.0 million of its investment in auction rate securities as long-term due to the uncertainty as to whether such securities will be available for current

operations. See note 3 for additional details on the Company's investment portfolio and events that occurred subsequent to December 31, 2007 that impacted the classification of auction rate securities in the Company's balance sheet.

All other available-for-sale investments are classified as short- or long-term investments according to their contractual maturities.

***Restricted Cash***

In accordance with the terms of the Company's line of credit agreement with General Electric Capital Corporation (GE Capital), the Company is obligated to maintain a certificate of deposit with the lender. The

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**CYTOKINETICS, INCORPORATED**  
**(A Development Stage Enterprise)**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

balance of the certificate of deposit was \$5.2 million and \$6.0 million at December 31, 2007 and 2006, respectively, and was classified as restricted cash.

***Fair Value of Financial Instruments***

For financial instruments consisting of cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities included in the Company's financial statements, the carrying amounts are reasonable estimates of fair value due to their short maturities. Estimated fair values for marketable securities, which are separately disclosed in Note 3, Investments, are based on quoted market prices for the same or similar instruments. Based on borrowing rates currently available to the Company, the fair value of the equipment financing lines is \$8.5 million compared to the book value of \$8.7 million.

***Property and Equipment***

Property and equipment are stated at cost and depreciated on a straight-line basis over the estimated useful lives of the related assets, which are generally three years for computer equipment and software, five years for laboratory equipment and office equipment, and seven years for furniture and fixtures. Amortization of leasehold improvements is computed using the straight-line method over the shorter of the remaining lease term or the estimated useful life of the related assets, typically ranging from three to seven years. Upon sale or retirement of assets, the costs and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in operations. Maintenance and repairs are charged to operations as incurred.

***Impairment of Long-lived Assets***

In accordance with the provisions of Statement of Financial Accounting Standards (SFAS) No. 144, Accounting for the Impairment or Disposal of Long-lived Assets, the Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Under SFAS No. 144, an impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is measured as the amount by which the carrying amount of a long-lived asset exceeds its fair value. Through December 31, 2007, there have been no such impairments.

***Revenue Recognition***

The Company recognizes revenue in accordance with SEC Staff Accounting Bulletin (SAB) No. 104, Revenue Recognition. SAB No. 104 requires that basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured. Determination of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fee charged for research performed and milestones met, and the collectability of those fees. Should changes in conditions cause management to determine these criteria are not met for certain future transactions, revenue recognized for any reporting period could be adversely affected.

Research and development revenues, which are earned under agreements with third parties for contract research and development activities, may include nonrefundable license fees, research and development funding, cost reimbursements and contingent milestones and royalties. The Company's revenue arrangements with multiple elements are evaluated under Emerging Issues Task Force ( EITF ) Issue No. 00-21, Revenue Arrangements with Multiple Deliverables, and are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer and whether there is objective and reliable evidence of the fair value of the undelivered items. The consideration the Company receives is allocated among the separate units based on their respective fair values, and the applicable revenue recognition criteria are applied to each of the separate units. Nonrefundable license fees are recognized as revenue as the Company performs under the

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applicable agreement. Where the level of effort is relatively consistent over the performance period, the Company recognizes total fixed or determined revenue on a straight-line basis over the estimated period of expected performance.

The Company recognizes milestone payments as revenue upon achievement of the milestone provided the milestone payment is nonrefundable, substantive effort and risk is involved in achieving the milestone and the amount of the milestone is reasonable in relation to the effort expended or risk associated with the achievement of the milestone. If these conditions are not met, the Company defers the milestone payment and recognizes it as revenue over the estimated period of performance under the contract as the Company completes its performance obligations.

Research and development revenues and cost reimbursements are based upon negotiated rates for full time employee equivalents ( FTE ) of the Company and actual out-of-pocket costs. Rates for FTEs are intended to approximate the Company's anticipated costs. Any amounts received in advance of performance are recorded as deferred revenue. None of the revenues recognized to date are refundable if the relevant research effort is not successful. In revenue arrangements in which both parties make payments to each other, the Company will evaluate the payments in accordance with the provisions of EITF Issue No. 01-9, Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor's Products) to determine whether payments made by us will be recognized as a reduction of revenue or as expense. In accordance with EITF Issue No. 01-9, revenue recognized by the Company may be reduced by payments made to the other party under the arrangement unless the Company receives a separate and identifiable benefit in exchange for the payments and the Company can reasonably estimate the fair value of the benefit received. The application of EITF Issue No. 01-9 has had no impact to the Company.

Grant revenues are recorded as research is performed and are not refundable.

***Preclinical Study and Clinical Trial Accruals***

A substantial portion of the Company's preclinical studies and all of the Company's clinical trials have been performed by third-party contract research organizations ( CROs ) and other vendors. For preclinical studies, the significant factors used in estimating accruals include the percentage of work completed to date and contract milestones achieved. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, duration of enrollment and percentage of work completed to date. The Company monitors patient enrollment levels and related activities to the extent possible through internal reviews, correspondence and status meetings with CROs, and review of contractual terms. The Company's estimates are dependent on the timeliness and accuracy of data provided by its CROs and other vendors. If the Company has incomplete or inaccurate data, it may under- or overestimate activity levels associated with various studies or trials at a given point in time. In this event, it could record adjustments to research and development expenses in future periods when the actual activity level become known. No material adjustments to preclinical study and clinical trial expenses have been recognized to date.

***Research and Development Expenditures***

Research and development costs are charged to operations as incurred.

***Retirement Plan***

The Company sponsors a 401(k) defined contribution plan covering all employees. There have been no employer contributions to the plan since inception.

*Income Taxes*

The Company accounts for income taxes under the liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and

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liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

In June 2006, the Financial Accounting Standards Board ( FASB ) issued Financial Interpretation No. 48 ( FIN 48 ), Accounting for Uncertainty in Income Taxes, which prescribes a recognition threshold and measurement process for recording in the financial statements uncertain tax positions taken or expected to be taken in a tax return. Additionally, FIN 48 provides guidance on the derecognition, classification, accounting in interim periods and disclosure requirements for uncertain tax positions. The accounting provisions of FIN 48 were effective for the Company beginning January 1, 2007. See Note 11 for additional information, including the effects of adoption on the Company's condensed consolidated financial statements.

***Comprehensive Income***

SFAS 130, *Reporting Comprehensive Income*, establishes standards for the reporting and presentation of comprehensive income and its components. Comprehensive income, as defined, includes all changes in stockholders equity during a period from non-owner sources. Comprehensive income for the years ended December 31, 2007, 2006 and 2005 was equal to net income adjusted for unrealized gains and losses on investments.

***Segment Reporting***

The Company has determined that it operates in only one segment.

***Net Loss Per Common Share***

Basic net loss per common share is computed by dividing net loss by the weighted average number of vested common shares outstanding during the period. Diluted net loss per common share is computed by giving effect to all potential dilutive common shares, including outstanding options, common stock subject to repurchase, warrants and convertible preferred stock unless their inclusion is anti-dilutive. A reconciliation of the numerator and denominator used in the calculation of basic and diluted net loss per common share follows (in thousands):

|  | <b>Years Ended December 31,</b> |             |             |
|--|---------------------------------|-------------|-------------|
|  | <b>2007</b>                     | <b>2006</b> | <b>2005</b> |
| Numerator:   |                                 |             |             |
| Net loss   | \$ (48,894)                     | \$ (57,115) | \$ (42,252) |
| Denominator:   |                                 |             |             |
| Weighted-average number of common shares outstanding | 47,591                          | 36,634      | 28,648      |
| Less: Weighted-average shares subject to repurchase  | (1)                             | (16)        | (66)        |
|  | 47,590                          | 36,618      | 28,582      |

Weighted-average number of common shares used in computing basic  
and diluted net loss per share

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The following outstanding options, common stock subject to repurchase, warrants and shares issuable under the Employee Stock Purchase Plan ( ESPP ) were excluded from the computation of diluted net loss per common share for the periods presented because including them would have had an antidilutive effect (in thousands):

|                                     | <b>Years Ended December 31,</b> |             |             |
|-------------------------------------|---------------------------------|-------------|-------------|
|                                     | <b>2007</b>                     | <b>2006</b> | <b>2005</b> |
| Options to purchase common stock    | 5,060                           | 4,033       | 3,282       |
| Common stock subject to repurchase  |                                 | 3           | 34          |
| Warrants to purchase common stock   | 474                             | 244         | 294         |
| Shares issuable related to the ESPP | 36                              | 43          | 41          |
| <br>Total shares                    | <br>5,570                       | <br>4,323   | <br>3,651   |

***Stock-based Compensation***

Effective January 1, 2006, the Company adopted the provisions of SFAS No. 123R, Share-Based Payment, which establishes accounting for share-based payment awards made to employees and directors including employee stock options and employee stock purchases. Under the provisions of SFAS No. 123R, stock-based compensation cost is measured at the grant date based on the calculated fair value of the award, and is recognized as an expense on a straight-line basis over the employee's requisite service period, generally the vesting period of the award. The Company elected the modified prospective transition method for awards granted subsequent to April 29, 2004, the date of its IPO, and the prospective transition method for awards granted prior to its IPO. Prior periods are not revised for comparative purposes under either transition method. The following table summarizes stock-based compensation related to employee stock options and employee stock purchases under SFAS No. 123R, including amortization of deferred compensation recognized under Accounting Principles Board Opinion No. 25 ( APB 25 ), Accounting for Stock Issued to Employees (in thousands):

|   | <b>Years Ended</b>  |              |
|---|---------------------|--------------|
|   | <b>December 31.</b> |              |
|   | <b>2007</b>         | <b>2006</b>  |
| Research and development                                    | \$ 2,932            | \$ 2,532     |
| General and administrative                                  | 2,621               | 2,111        |
| <br>Stock-based compensation included in operating expenses | <br>\$ 5,553        | <br>\$ 4,643 |

The Company uses the Black-Scholes option pricing model to determine the fair value of stock options and employee stock purchase plan shares. The key input assumptions used to estimate fair value of these awards include the exercise

price of the award, the expected option term, the expected volatility of the Company's stock over the option's expected term, the risk-free interest rate over the option's expected term, and the Company's expected dividend yield, if any.

The fair value of share-based payments was estimated on the date of grant using the Black-Scholes option pricing model based on the following weighted average assumptions:

|                          | <b>Year Ended<br/>December 31, 2007</b> |             | <b>Year Ended<br/>December 31, 2006</b> |             |
|--------------------------|---|-------------|---|-------------|
|                          | <b>Employee<br/>Stock<br/>Options</b>   | <b>ESPP</b> | <b>Employee<br/>Stock<br/>Options</b>   | <b>ESPP</b> |
| Risk-free interest rate  | 4.49%                                   | 4.33%       | 4.68%                                   | 4.91%       |
| Volatility               | 73%                                     | 76%         | 74%                                     | 72%         |
| Expected life (in years) | 6.00                                    | 1.25        | 6.08                                    | 1.25        |
| Expected dividend yield  | 0.00%                                   | 0.00%       | 0.00%                                   | 0.00%       |

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The Company estimates the expected term of options granted by taking the average of the vesting term and the contractual term of the options, referred to as the simplified method in accordance with SAB No. 107, Share-Based Payment. The Company estimates the volatility of our common stock by using an average of historical stock price volatility of comparable companies. The risk-free interest rate that the Company uses in the option pricing model is based on the U.S. Treasury zero-coupon issues with remaining terms similar to the expected terms of the options. The Company does not anticipate paying dividends in the foreseeable future and therefore uses an expected dividend yield of zero in the option pricing model. The Company is required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. Historical data is used to estimate pre-vesting option forfeitures and record stock-based compensation expense only on those awards that are expected to vest.

As a result of adopting SFAS No. 123R on January 1, 2006, the Company's net loss for the years ended December 31, 2007 and 2006 was \$4.8 million and \$3.4 million larger, respectively, than if it had continued to account for stock-based compensation under APB 25. Reported basic and diluted net loss per common share for the year ended December 31, 2007 was \$1.03, and would have been \$0.93 per share if the Company had continued to account for stock-based compensation under APB 25. Reported basic and diluted net loss per common share for the year ended December 31, 2006 was \$1.56 and would have been \$1.47 per share if the Company had continued to account for stock-based compensation under APB 25.

As of December 31, 2007, there was \$10.3 million of total unrecognized compensation cost related to non-vested stock-based compensation arrangements granted under the Company's stock option plans under SFAS No. 123R, which is expected to be recognized over a weighted-average period of 2.6 years.

The Company amortizes deferred stock-based compensation recorded prior to the adoption of SFAS No. 123R for stock options granted prior to its IPO. Fair value of these awards has been calculated at grant date using the intrinsic value method as prescribed in APB 25. At December 31, 2007, the balance of deferred stock based compensation was \$329,000, which the Company expects to amortize to expense in the year ending December 31, 2008.

Prior to January 1, 2006, the Company accounted for stock-based compensation to employees in accordance with APB No. 25 and related interpretations. The Company also followed the disclosure requirements of SFAS No. 123, Accounting for Stock-Based Compensation, and complied with the disclosure requirements of SFAS No. 148, Accounting for Stock-Based Compensation Transition and Disclosure: an Amendment of FASB Statement No. 123. The following table illustrates the effects on net loss and loss per share for the year ended December 31, 2005 as if the Company had applied the fair value recognition provisions of SFAS No. 123 to all stock-based employee awards. (in thousands, except per share data):

|   | <b>Year Ended<br/>December 31, 2005</b> |
|---|---|
| Net loss, as reported   | \$ (42,252)                             |
| Deduct: Total stock-based employee compensation determined under fair value based method for all awards | (1,947)                                 |

|   |    |          |
|---|----|----------|
| Adjusted net loss                             | \$ | (44,199) |
| Net loss per common share, basic and diluted: |    |          |
| As reported                                   | \$ | (1.48)   |
| Adjusted                                      | \$ | (1.55)   |

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The value of each employee stock option granted is estimated on the date of grant under the fair value method using the Black-Scholes option pricing model. The value of share-based payments was estimated based the following weighted average assumptions:

|                          | <b>Employee<br/>Stock<br/>Options<br/>Year Ended December 31,<br/>2005</b> | <b>ESPP<br/>Year Ended December 31,<br/>2005</b> |
|--------------------------|--|--|
| Risk-free interest rate  | 4.18%  | 3.47%  |
| Volatility               | 78%  | 79%  |
| Expected life (in years) | 5.0  | 1.25   |
| Expected dividend yield  | 0.00%  | 0.00%  |

On November 10, 2005, the FASB issued FASB Staff Position No. 123R-3, Transition Election Related to Accounting for Tax Effects of Share-Based Payment Awards ( FSP FAS 123R-3 ). The Company has elected to adopt the alternative transition method provided in FSP FAS 123R-3. The alternative transition method includes a simplified method to establish the beginning balance of the additional paid-in capital pool related to the tax effects of employee share-based payments, which is available to absorb tax deficiencies recognized subsequent to the adoption of SFAS No. 123R.

***Recent Accounting Pronouncements***

In September 2006, the FASB issued SFAS No. 157, Fair Value Measurements. This standard defines fair value, establishes a framework for measuring fair value in accounting principles generally accepted in the United States of America, and expands disclosure about fair value measurements. This pronouncement applies under the other accounting standards that require or permit fair value measurements. Accordingly, this statement does not require any new fair value measurement. SFAS No. 157 is effective for fiscal years beginning after November 15, 2007 and interim periods within those fiscal years, for all financial assets and liabilities and for nonfinancial assets and liabilities that are recognized or disclosed at fair value at least annually. It is effective for fiscal years beginning after November 15, 2008 for all other nonfinancial assets and liabilities. SFAS No. 157 is to be applied prospectively. The Company does not expect that the adoption of the requirements of SFAS No. 157 that are effective on January 1, 2008 will have a material impact on its financial position or results of operations. The Company is currently evaluating the requirements of SFAS No. 157 that will become effective for it on January 1, 2009, and has not yet determined the impact, if any, on the financial statements.

In February 2007, the FASB issued SFAS No. 159, The Fair Value Option for Financial Assets and Financial Liabilities, which permits entities to choose to measure many financial instruments and certain other items at fair value that are not currently required to be measured at fair value. SFAS No. 159 is effective for the Company on January 1, 2008. The Company does not expect that the adoption of SFAS 159 will have a material impact on its financial position or results of operations.

In June 2007, the EITF reached a consensus on EITF Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities*. EITF Issue No. 07-3 states that nonrefundable advance payments for future research and development activities should be deferred and recognized as an expense as the goods are delivered or the related services are performed. Entities should then continue to evaluate whether they expect the goods to be delivered or services to be rendered and, if an entity does not expect the goods to be delivered or services to be rendered, the capitalized advance payment should be charged to expense. EITF Issue No. 07-3 will be effective for the Company on January 1, 2008 and is to be applied prospectively for new contracts entered into on or after the effective date. The Company is currently evaluating the impact on its financial statements of adopting EITF Issue No. 07-3.

In November 2007, the EITF issued a consensus on EITF Issue No. 07-01, *Accounting for Collaboration Arrangements Related to the Development and Commercialization of Intellectual Property*, which is focused on how the parties to a collaborative agreement should account for costs incurred and revenue generated on sales to

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third parties, how sharing payments pursuant to a collaboration agreement should be presented in the income statement and certain related disclosure questions. EITF Issue No. 07-01 is to be applied retrospectively for collaboration arrangements in fiscal years beginning after December 15, 2008. The Company is currently evaluating the impact on its financial statements of adopting EITF Issue No. 07-1.

In December 2007, the SEC issued SAB No. 110 ( SAB No. 110 ), which addresses the continued use of the simplified method for estimating the expected term for stock based compensation. Previously, under SAB No. 107, the use of the simplified method was intended to be discontinued after December 31, 2007. Under SAB No. 110, companies may continue to use the simplified method in certain circumstances. The Company has used the simplified method of estimating the expected term for stock based compensation since its adoption of SFAS No. 123R on January 1, 2006, and is in the process of determining the effect, if any, the adoption of SAB No. 110 on its financial statements.

**Note 2 Supplementary Cash Flow Data**

Supplemental cash flow information was as follows (in thousands):

|   | <b>Years Ended December 31,</b> |             |             | <b>Period from</b>         |
|---|---------------------------------|-------------|-------------|----------------------------|
|   | <b>2007</b>                     | <b>2006</b> | <b>2005</b> | <b>August 5, 1997</b>      |
|   |                                 |             |             | <b>(Date of Inception)</b> |
|   |                                 |             |             | <b>to</b>                  |
|   |                                 |             |             | <b>December 31, 2007</b>   |
| Cash paid for interest  | \$ 594                          | \$ 439      | \$ 417      | \$ 3,587                   |
| Cash paid for income taxes  | 1                               | 1           | 1           | 10                         |
| Significant non-cash investing and financing activities:                                      |                                 |             |             |                            |
| Deferred stock-based compensation   |                                 |             |             | 6,940                      |
| Purchases of property and equipment through accounts payable                                  | 359                             | 1,554       | 843         | 359                        |
| Purchases of property and equipment through trade in value of disposed property and equipment |                                 | 131         | 2           | 258                        |
| Penalty on restructuring of equipment financing lines   |                                 |             |             | 475                        |
| Conversion of convertible preferred stock to common stock                                     |                                 |             |             | 133,172                    |

**Note 3 Investments**

The amortized cost and fair value of short- and long-term investments at December 31, 2007 and 2006 were as follows (in thousands):

**December 31, 2007**

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|                              | <b>Amortized<br/>Cost</b> | <b>Unrealized<br/>Gains</b> | <b>Unrealized<br/>Losses</b> | <b>Fair<br/>Value</b> | <b>Maturity<br/>Dates</b> |
|------------------------------|---------------------------|-----------------------------|------------------------------|-----------------------|---------------------------|
| Short-term investments:      |                           |                             |                              |                       |                           |
| Municipal bonds (taxable)    | \$ 3,175                  |                             |                              | \$ 3,175              | 1/2008                    |
| Total short-term investments | \$ 3,175                  | \$                          | \$                           | \$ 3,175              |                           |
| Long-term investments:       |                           |                             |                              |                       |                           |
| Municipal bonds (taxable)    | \$ 20,025                 |                             |                              | \$ 20,025             | 6/2036 8/2045             |
| Total long-term investments  | \$ 20,025                 | \$                          | \$                           | \$ 20,025             |                           |



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|                              | <b>December 31, 2006</b> |                   |                   |              | <b>Maturity</b> |        |
|------------------------------|--------------------------|-------------------|-------------------|--------------|-----------------|--------|
|                              | <b>Amortized</b>         | <b>Unrealized</b> | <b>Unrealized</b> | <b>Fair</b>  | <b>Dates</b>    |        |
|                              | <b>Cost</b>              | <b>Gains</b>      | <b>Losses</b>     | <b>Value</b> |                 |        |
| Short-term investments:      |                          |                   |                   |              |                 |        |
| US corporate bonds           | \$ 24,325                | \$ 1              | \$ (21)           | \$ 24,305    | 1/2007          | 6/2007 |
| Government agencies bonds    | 15,987                   |                   | (37)              | 15,950       | 1/2007          | 5/2007 |
| Municipal bonds (taxable)    | 29,900                   |                   |                   | 29,900       |                 | 1/2007 |
| Total short-term investments | \$ 70,212                | \$ 1              | \$ (58)           | \$ 70,155    |                 |        |

Our auction rate securities, which are included in municipal bonds and totaled \$23.2 million as of December 31, 2007 and \$29.9 million as of December 31, 2006, are securities that are structured with short-term interest reset dates of less than 30 days but with maturities generally greater than 10 years. At the end of each reset period, investors can attempt to sell or continue to hold the securities at par value. \$20.0 million of these auction rate securities were classified as long-term investments as of December 31, 2007 based on their legal stated maturity date.

Market values were determined for each individual security in the investment portfolio based on quoted market prices. The unrealized losses related to these investments are attributed to changes in interest rates and are considered to be temporary in nature. As of December 31, 2007, there were no auction rate securities in an unrealized loss position and there were no failed auctions associated with the Company's auction rate securities through that date. In January 2008, the Company's auction rate securities with January auction reset dates had successful auctions at which their interest rates were reset. In February 2008, the Company liquidated \$3.2 million of its auction rate securities at par, which were classified as short-term investment as of December 31, 2007. As of March 4, 2008, \$20.0 million of auction rate securities remained in the Company's portfolio and auctions for these securities failed in February and early March 2008. As a result, these auction rate securities were classified as long-term investments. These failures resulted in the interest rates on these investments resetting to contractually stipulated "fail rates" that are variable based on short-term municipal bond or other market indices, or fixed rates that may result in the Company earning above-market interest rates on these investments. If the Company needs to access these funds, it will not be able to do so until a future auction on these investments is successful, the issuer redeems the outstanding securities, the securities mature or the Company sells the securities in the secondary market. As a result of this development and remaining uncertainty in the market for auction rate securities, the Company has classified \$20.0 million of auction rate securities as "long-term" in the accompanying balance sheet as of December 31, 2007.

Interest income was \$8.3 million, \$4.7 million and \$2.9 million for the years ended December 31, 2007, 2006 and 2005, respectively, and \$24.3 million for the period August 5, 1997 (inception) through December 31, 2007.

As of December 31, 2007, the Company's short- and long-term investments had no unrealized gain or loss.

As of December 31, 2006, none of the Company's short-term investments had been in a continuous loss position, and none of its investments with unrealized losses of less than twelve months were deemed to be other-than-temporarily

impaired. The unrealized losses on the Company's investments in U.S. corporate and U.S. government agencies bonds at December 31, 2006 were primarily caused by rising interest rates. The Company was able to collect all contractual cash flows related to the U.S. corporate bonds and U.S. government agencies bonds held at December 31, 2006 and no realized losses were incurred.

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|   | <b>December 31,</b> |             |
|---|---------------------|-------------|
|   | <b>2007</b>         | <b>2006</b> |
| Property and equipment, net (in thousands):     |                     |             |
| Laboratory equipment                            | \$ 19,081           | \$ 18,249   |
| Computer equipment and software                 | 3,647               | 3,692       |
| Office equipment, furniture and fixtures        | 365                 | 368         |
| Leasehold improvements                          | 3,054               | 2,796       |
|   | 26,147              | 25,105      |
| Less: Accumulated depreciation and amortization | (18,419)            | (15,903)    |
|   | \$ 7,728            | \$ 9,202    |

Property and equipment pledged as collateral against outstanding borrowings under the Company's equipment financing lines totaled \$21.9 million, less accumulated depreciation of \$15.6 million, at December 31, 2007 and \$18.1 million, less accumulated depreciation of \$13.2 million, at December 31, 2006.

|                                     | <b>December 31,</b> |             |
|-------------------------------------|---------------------|-------------|
|                                     | <b>2007</b>         | <b>2006</b> |
| Accrued liabilities (in thousands): |                     |             |
| Consulting and professional fees    | \$ 5,178            | \$ 3,938    |
| Bonus                               | 1,560               | 1,336       |
| Vacation and other payroll related  | 1,211               | 1,222       |
| Other accrued expenses              | 609                 | 970         |
|                                     | \$ 8,558            | \$ 7,466    |

Interest receivable on cash equivalents and short-term investments of \$117,000 and \$53,000 is included in prepaid and other current assets at December 31, 2007 and 2006, respectively.

**Note 5 Related Party Transactions*****Research and Development Arrangements****GSK*

In 2001, the Company entered into a collaboration and license agreement with GSK, establishing a strategic alliance to discover, develop and commercialize small molecule drugs for the treatment of cancer and other diseases. Under this agreement, GSK paid the Company an upfront licensing fee for rights to certain technologies and milestone payments regarding performance and developments within agreed-upon projects. In conjunction with these projects, GSK agreed to reimburse the Company's costs associated with the strategic alliance. In connection with the agreement, in 2001 GSK made a \$14.0 million equity investment in the Company. In 2001, the Company also received \$14.0 million for the upfront licensing fee, which was recognized ratably over the initial five-year research term of the agreement. In the years ended December 31, 2007, 2006 and 2005, the Company recognized none, \$1.4 million, and \$2.8 million, respectively, as license revenue under this agreement. At December 31, 2007 and 2006, no license revenue under this agreement was deferred. The Company received and recognized as revenue \$0.4 million, \$1.6 million, and \$4.5 million in FTE and other expense reimbursements for the years ended December 31, 2007, 2006 and 2005, respectively, and \$32.3 million in the period from August 5, 1997 (inception) through December 31, 2007. The Company also received and recognized as revenue \$1.0 million, none, and \$0.5 million in performance milestone payments under the agreement for the years ended December 31,

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2007, 2006 and 2005, respectively, and \$8.0 million in the period from August 5, 1997 (inception) through December 31, 2007 as no ongoing performance obligations existed with respect to this aspect of the agreement.

For those drug candidates that GSK develops under the strategic alliance, the Company can elect to co-fund certain later-stage development activities which would increase its potential royalty rates on sales of resulting drugs and provide the Company with the option to secure co-promotion rights in North America. If the Company exercises its co-promotion option, then it is entitled to receive reimbursement from GSK for certain sales force costs it incurs in support of its commercial activities.

Under the November 2006 amendment to the collaboration and license agreement with GSK, the Company assumed responsibility, at its expense, for the continued research, development and commercialization of inhibitors of kinesin spindle proteins, including ispinesib and SB-743921, and other mitotic kinesins. Under the November 2006 amendment, the Company's development of ispinesib and SB-743921 is subject to GSK's option to resume responsibility for the development and commercialization of either or both drug candidates, exercisable during a defined period. If GSK exercises its option for a drug candidate, it will pay the Company an option fee equal to the costs the Company independently incurred for that drug candidate, plus a premium intended to compensate for the cost of capital associated with such costs, subject to an agreed limit for such costs and premium. Upon GSK exercising its option for a drug candidate, the Company may receive additional pre-commercialization milestone payments with respect to such drug candidate and increased royalties on net sales of any resulting product, in each case, beyond those contemplated under the original agreement. If GSK does not exercise its option for a drug candidate, the Company will be obligated to pay royalties to GSK on the sales of any resulting products. The November 2006 amendment supersedes a previous amendment to the collaboration and license agreement dated September 2005, which specifically related to SB-743921. Accrued liabilities at December 31, 2007 include \$20,000 payable to GSK for outsourced services.

GSK and the Company are conducting translational research activities focused to CENP-E, which are coordinated under an agreed joint research program during an extended research term under the June 2006 and June 2007 amendments to the collaboration and license agreement. GSK is currently conducting a Phase I clinical trial of the CENP-E inhibitor GSK-923295 under the agreement.

GSK made additional equity investments in the Company in 2003 and 2004 of \$3.0 million and \$7.0 million, respectively.

*Amgen*

On December 29, 2006, the Company entered into a collaboration and option agreement with Amgen to discover, develop and commercialize novel small-molecule therapeutics that activate cardiac muscle contractility for potential applications in the treatment of heart failure. The agreement provides a non-exclusive license and access to certain technology, as well as providing Amgen an option to participate in future development and commercialization of the CK-1827452 world-wide, excluding Japan. Under the terms of the agreement, the Company received an upfront, non-refundable license and technology access fee of \$42.0 million from Amgen, which the Company is recognizing as revenue ratably over the maximum term of the non-exclusive license, which is four years. Management determined that the obligations under the non-exclusive license did not meet the requirement for separate units of accounting and

therefore should be recognized as a single unit of accounting.

During the initial research term of the collaboration and option agreement, in addition to performing research at our own expense, the Company conducts all development activities at its own expense for CK-1827452 in accordance with an agreed upon development plan. Amgen's option is exercisable during a defined period, the ending of which is dependent upon satisfaction of certain conditions, primarily the delivery of Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed development plan, the results from which may be sufficient to support its progression into Phase IIb clinical development. To exercise its option, Amgen is required to pay a non-refundable fee of \$50.0 million and thereafter would have an exclusive license. On exercise of the option, the Company is required to transfer all data and know-how necessary to enable Amgen to assume responsibility for

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development and commercialization of CK-1827452 and related compounds, which Amgen will perform at its sole expense. Development services, if any, performed by the Company after commencement of the exclusive license term will be reimbursed by Amgen. Under the terms of the agreement, the Company may be eligible to receive pre-commercialization and commercialization milestone payments of up to \$600.0 million in the aggregate on CK-1827452 and other potential products arising from research under the collaboration as well as royalties that escalate based on increasing levels of the annual net sales of products commercialized under the agreement. The agreement also provides for the Company to receive increased royalties by co-funding Phase III development costs of drug candidates under the collaboration. If the Company elects to co-fund such costs, it would be entitled to co-promote products in North America and participate in agreed commercial activities in institutional care settings, at Amgen's expense. If Amgen elects not to exercise its option on CK-1827452, the Company may then proceed to independently develop CK-1827452 and the research collaboration would terminate.

In connection with entering into the collaboration and option agreement, the Company also entered into a common stock purchase agreement (the "CSPA") with Amgen, which provided for the sale of 3,484,806 shares of the Company's Common Stock at a price per share of \$9.47 and an aggregate purchase price of approximately \$33.0 million. On January 2, 2007, the Company issued 3,484,806 shares of common stock to Amgen under the CSPA. After deducting the offering costs, we received net proceeds of approximately \$32.9 million in January 2007. The common stock was valued using the closing price of the common stock on December 29, 2006, the last trading day of the common stock prior to issuance. The difference between the price paid by Amgen of \$9.47 per share and the stock price of \$7.48 per share of common stock totaled \$6.9 million. This premium was recorded as deferred revenue in January 2007 and is being recognized as revenue ratably over the maximum term of the non-exclusive license granted to Amgen under the collaboration and option agreement, which is approximately four years.

In 2007 and 2006, the Company recognized \$12.2 million and \$0.1 million respectively in license revenue under the agreement.

*Other Research and Development Arrangements*

In 1998, the Company entered into a licensing agreement with certain universities where the Company's founding scientists are also affiliates of the universities. The Company agreed to pay technology license fees, as well as milestone payments for technology developed under the licensing agreement. The Company is also obligated to make minimum royalty payments, as specified in the agreement, commencing the year of product market introduction or upon an agreed upon anniversary of the licensing agreement. The Company paid \$74,000, \$59,000 and \$67,000 to the universities under this agreement in 2007, 2006 and 2005, respectively, and \$1.1 million in the period August 5, 1997 (inception) through December 31, 2007.

*Other*

In August 2004, the Company entered into a collaboration and facilities agreement with Portola Pharmaceuticals, Inc. ("Portola"), replacing a verbal agreement entered into in December 2003. Under the agreement, Portola provided research and related services and access to a portion of their facilities to support such services. Charles J. Homcy, M.D., is the President and CEO of Portola, a member of the Company's Board of Directors and a consultant to the Company. In the years ended December 31, 2007, 2006 and 2005, the Company incurred expenses of \$164,000,

\$913,000, and \$1.4 million, respectively, for research services provided under this agreement. In March 2005, the agreement was amended to provide for the purchase and use of certain equipment by Portola in connection with Portola providing research and related services to the Company and the Company's reimbursement to Portola of \$285,000 for the equipment in eight quarterly payments from January 2006 through October 2007. The entire equipment reimbursement of \$285,000 was recognized in expenses in 2005. In March 2006, the agreement was amended to extend it through December 31, 2006 and update certain pricing and other terms and conditions. Accounts payable and accrued liabilities at December 31, 2007 and 2006 included none and \$164,000, respectively, payable to Portola for such services. The Company also incurred consulting fees to Dr. Homcy of \$23,000 in 2007



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and \$25,000 in each of 2006 and 2005. Accrued liabilities at December 31, 2007 included \$2,500 payable to Dr. Homcy for consulting fees.

In August 2006, the Company entered into an agreement with Portola whereby Portola sub-subleased approximately 2,500 square feet of office space from the Company at a monthly rate of \$1.75 per square foot. The term of the agreement commenced on August 22, 2006 and continued until October 31, 2006, with the option to extend on a month-to-month basis thereafter. Sublease income from this agreement offsets rent expense. Portola terminated the sublease agreement effective April 30, 2007.

In 2001 and 2002, the Company extended loans for \$200,000 and \$100,000, respectively, to certain officers of the Company. The loans accrue interest at 5.18% and 5.75% and are scheduled to mature on November 12, 2010 and July 12, 2008, respectively. In 2002 the Company extended loans totaling \$650,000 to various certain officers and employees of the Company. The loans accrue interest at rates ranging from 4.88% to 5.80% and have scheduled maturities on various dates between 2005 and 2011. Certain of the loans are collateralized by the common stock of the Company owned by the officers and by stock options and were repaid in full no later than eighteen months after the Company's IPO date of April 29, 2004. Certain of the loans will be forgiven if the officers remain with the Company through the maturation of their respective loans. The Company did not extend any loans to officers or employees of the Company subsequent to 2002. Principal repayments totaled \$129,000 and \$63,000 and principal forgiven totaled \$97,000 and \$88,000 in 2007 and 2006, respectively. A total of \$226,000 and \$451,000 was outstanding on these loans at December 31, 2007 and 2006 and was classified as related party notes receivable. Interest receivable on these loans totaled \$3,000 at December 31, 2007 and \$5,000 at December 31, 2006 and was included in related party accounts receivable.

**Note 6 Other Research and Development Arrangements**

In 2003, the Company entered into a strategic alliance with AstraZeneca to develop a new application of the Company's Cytometri<sup>®</sup> technology. Under the agreement, AstraZeneca agreed to reimburse certain of the Company's costs over a two-year research term, pay licensing fees to the Company, and, upon the successful achievement of certain agreed-upon performance criteria, make a milestone payment to the Company. The Company received and recognized FTE reimbursements of none in the years ended December 31, 2007 and 2006, \$1.1 million in the year ended December 31, 2005 and \$2.4 million in the period from August 5, 1997 (inception) through December 31, 2007. The research term of the collaboration and license agreement with AstraZeneca expired in December 2005, and the agreement was formally terminated in August 2006.

**Note 7 Equipment Financing Line**

In July 2002, the Company entered into a financing agreement with GE Capital under which the Company could borrow up to \$7.5 million through a financing line of credit, which was subsequently refinanced. In 2002, 2003 and 2004 the Company executed draws on this line of credit totaling approximately \$7.5 million with effective interest rates ranging from 4.25% to 8.77%. This financing line of credit expired on January 1, 2004 and no additional borrowings are available to the Company under it. As of December 31, 2007, the balance of equipment loans outstanding under this line was approximately \$2.5 million.

In January 2004, the Company entered into a financing agreement with GE Capital under which the Company could borrow up to \$4.5 million under a financing line of credit expiring December 31, 2006. The Company executed draws aggregating \$2.0 million, \$1.3 million and \$0.9 million during 2006, 2005 and 2004, respectively at interest rates ranging from 4.56% to 7.44%. In October 2006, the Company was informed by GE Capital that the amounts available under this equipment line had been reduced by approximately \$0.3 million. As of December 31, 2007, the balance of equipment loans outstanding under this line was \$2.8 million, and no additional borrowings are available to the Company.

In April 2006, the Company obtained a line of credit with GE Capital of up to \$4.6 million to finance certain equipment until April 28, 2007. In 2007 and 2006, the Company executed draws on this line of credit totaling

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approximately \$4.1 million at interest rates ranging from 7.24% to 7.68%. As of December 31, 2007, the balance of equipment loans outstanding under this line was \$3.4 million and no additional borrowings are available to the Company under it.

In August 2007, the Company secured a new line of credit with GE Capital of up to \$3.0 million to finance certain equipment until September 30, 2008. The line of credit is subject to the terms of a Master Security Agreement between the Company and GE Capital, dated February 2001 and as amended March 24, 2005 ( MSA ) and related term sheet. As of December 31, 2007, the Company had not borrowed any funds under this line.

Borrowings under the equipment lines have financing terms ranging from 48 to 60 months. All lines are subject to the MSA between the Company and GE Capital and are collateralized by property and equipment of the Company purchased by such borrowed funds and other collateral as agreed to be the Company. In connection with the lines of credit with GE Capital, the Company is obligated to maintain a certificate of deposit with the lender (see Note 1 Organization and Summary of Significant Accounting Policies *Restricted Cash* ).

As of December 31, 2007, future minimum lease payments under equipment lease lines were as follows (in thousands):

|            |          |
|------------|----------|
| 2008       | \$ 4,050 |
| 2009       | 2,025    |
| 2010       | 1,629    |
| 2011       | 833      |
| 2012       | 152      |
| Thereafter |          |
| Total      | \$ 8,689 |

Interest expense was \$0.7 million, \$0.5 million, and \$0.5 million for the years ended December 31, 2007, 2006, and 2005, respectively, and \$4.3 million for the period from August 5, 1997 (date of inception) through December 31, 2007.

**Note 8 Commitments and Contingencies**

***Leases***

The Company leases office space and equipment under two non-cancelable operating leases with expiration dates in 2011 and 2013. Rent expense net of sublease income was \$3.2 million, \$3.0 million, and \$2.2 million for the years ended December 31, 2007, 2006, and 2005, respectively, and was \$18.3 million for the period from August 5, 1997 (inception) through December 31, 2007. The terms of both facility leases provide for rental payments on a graduated scale as well as the Company's payment of certain operating expenses. The Company recognizes rent expense on a straight-line basis over the lease period. In 2006, the Company entered into a sublease agreement with Portola, which

resulted in \$18,000 and \$22,000 of sublease income offsetting rent expense in 2007 and 2006, respectively.

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As of December 31, 2007, future minimum lease payments under noncancelable operating leases were as follows (in thousands):

|            |           |
|------------|-----------|
| 2008       | \$ 3,256  |
| 2009       | 3,202     |
| 2010       | 3,296     |
| 2011       | 2,734     |
| 2012       | 2,077     |
| Thereafter | 1,329     |
| Total      | \$ 15,894 |

In the ordinary course of business, the Company may provide indemnifications of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters, including, but not limited to, losses arising out of the Company's breach of such agreements, services to be provided by or on behalf of the Company, or from intellectual property infringement claims made by third-parties. In addition, the Company has entered into indemnification agreements with its directors and certain of its officers and employees that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. The Company maintains director and officer insurance, which may cover certain liabilities arising from its obligation to indemnify its directors and certain of its officers and employees, and former officers and directors in certain circumstances. The Company maintains product liability insurance and comprehensive general liability insurance, which may cover certain liabilities arising from its obligations to indemnify third parties. It is not possible to determine the maximum potential amount of exposure under these indemnifications and indemnification agreements due to the limited history of prior indemnification claims and the unique facts and circumstances involved in each particular indemnification or indemnification agreement. Such indemnifications and indemnification agreements may not be subject to maximum loss clauses.

**Note 9 Convertible Preferred Stock**

Effective upon the closing of the initial public offering on April 29, 2004, all outstanding shares of the convertible preferred stock converted into 17,062,145 shares of common stock. In January 2004, the Board of Directors approved an amendment to the Company's amended and restated certificate of incorporation changing the authorized number of shares of preferred stock to 10,000,000, effective upon the closing of the initial public offering. As of December 31, 2007 and 2006, there were 10,000,000 shares of convertible preferred stock authorized and no shares outstanding.

**Note 10 Stockholders Equity (Deficit)*****Common Stock***

The Company's Registration Statement (SEC File No. 333-112261) for its initial public offering was declared effective by the SEC on April 29, 2004 and the Company's common stock commenced trading on the NASDAQ National

Market, now the NASDAQ Global Market, on that date under the trading symbol CYTK. The Company sold 7,935,000 shares of common stock in the offering, including shares that were issued upon the full exercise by the underwriters of their over-allotment option, at \$13.00 per share for aggregate gross proceeds of \$103.2 million. In connection with this offering, the Company paid underwriters' commissions of \$7.2 million and incurred offering expenses of \$2.0 million. After deducting the underwriters' commissions and the offering expenses, the Company received net proceeds of approximately \$94.0 million from the offering. In addition, pursuant to an agreement with an affiliate of GSK, the Company sold 538,461 shares of its common stock to GSK immediately prior to the closing of the initial public offering at a purchase price of \$13.00 per share, for a total of approximately \$7.0 million in net proceeds.

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In October 2005, the Company entered into a committed equity financing facility ( CEFF ) with Kingsbridge Capital Ltd. ( Kingsbridge ), pursuant to which Kingsbridge committed to purchase, subject to certain conditions of the CEFF, up to \$75.0 million of the Company s newly-issued common stock during the next three years. Subject to certain conditions and limitations, from time to time under the CEFF, the Company could require Kingsbridge to purchase newly-issued shares of the Company s common stock at a price between 90% and 94% of the volume weighted average price on each trading day during an eight day, forward-looking pricing period. The maximum number of shares the Company could issue in any pricing period is the lesser of 2.5% of the Company s market capitalization immediately prior to the commencement of the pricing period or \$15.0 million. The minimum acceptable volume weighted average price for determining the purchase price at which the Company s stock could be sold in any pricing period was the greater of \$3.50 or 85% of the closing price for the Company s common stock on the day prior to the commencement of the pricing period. In 2007, the Company received gross proceeds of \$9.5 million from the drawdown of 2,075,177 shares of common stock pursuant to our CEFF. In 2006, the Company received gross proceeds of \$17.0 million from the drawdown of 2,740,735 shares of common stock pursuant to our CEFF. In 2005, the Company received gross proceeds of \$5.7 million from the draw down and sale of 887,576 shares of common stock before offering costs of \$178,000. No further draw downs are available to the Company under the 2005 CEFF with Kingsbridge.

In January 2006, the Company entered into a stock purchase agreement with certain institutional investors relating to the issuance and sale of 5,000,000 shares of our common stock at a price of \$6.60 per share, for gross offering proceeds of \$33.0 million. In connection with this offering, the Company paid an advisory fee to a registered broker-dealer of \$1.0 million. After deducting the advisory fee and the offering costs, the Company received net proceeds of approximately \$32.0 million from the offering. The offering was made pursuant to the Company s shelf registration statement on Form S-3 (SEC File No. 333-125786) filed on June 14, 2005.

In December 2006, the Company entered into stock purchase agreements with selected institutional investors relating to the issuance and sale of 5,285,715 shares of our common stock at a price of \$7.00 per share, for gross offering proceeds of \$37.0 million. In connection with this offering, the Company paid placement agent fees to three registered broker-dealers totaling \$1.85 million. After deducting the placement agent fees and the offering costs, the Company received net proceeds of approximately \$34.9 million from the offering. The offering was made pursuant to the Company s shelf registration statements on Form S-3 (SEC File No. 333-125786) filed on June 14, 2005 and October 31, 2006 (SEC File No. 333-138306).

In connection with entering into the collaboration and option agreement, the Company also entered into a CSPA with Amgen, which provided for the sale of 3,484,806 shares of the Company s Common Stock at a price per share of \$9.47 and an aggregate purchase price of approximately \$33.0 million. On January 2, 2007, the Company issued 3,484,806 shares of common stock to Amgen under the CSPA. After deducting the offering costs, the Company received net proceeds of approximately \$32.9 million in January 2007. The common stock was valued using the closing price of the common stock on December 29, 2006, the last trading day of the common stock prior to issuance. The difference between the price paid by Amgen of \$9.47 per share and the stock price of \$7.48 per share of common stock totaled \$6.9 million. This premium was recorded as deferred revenue in January 2007 and is being recognized as revenue ratably over the maximum term of the non-exclusive license granted to Amgen under the collaboration and option agreement, which is approximately four years.

In October 2007, the Company entered into a new committed equity financing facility (the 2007 CEFF ) with Kingsbridge, pursuant to which Kingsbridge committed to finance up to \$75.0 million of capital over a three-year period. Subject to certain conditions and limitations, from time to time under the 2007 CEFF, at the Company's election, Kingsbridge is committed to purchase newly-issued shares of the Company's common stock at a price between 90% and 94% of the volume weighted average price on each trading day during an eight day, forward-looking pricing period. The maximum number of shares the Company may issue in any pricing period is the lesser of 2.5% of its market capitalization immediately prior to the commencement of the pricing period or \$15.0 million. As part of the arrangement, the Company issued a warrant to Kingsbridge to purchase 230,000 shares of the



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Company's common stock at a price of \$7.99 per share, which represents a premium over the closing price of its common stock on the date it entered into the 2007 CEFF. This warrant is exercisable beginning six months after the date of grant and for a period of three years thereafter. Under the terms of the 2007 CEFF, the maximum number of shares the Company may sell is 9,779,411 (exclusive of the shares underlying the warrant) which, under the rules of the NASDAQ Stock Market LLC, is approximately the maximum number of shares it may sell to Kingsbridge without approval of the Company's stockholders. This limitation may further limit the amount of proceeds the Company is able to obtain from the 2007 CEFF. The Company is not obligated to sell any of the \$75.0 million of common stock available under the 2007 CEFF and there are no minimum commitments or minimum use penalties. The 2007 CEFF does not contain any restrictions on the Company's operating activities, any automatic pricing resets or any minimum market volume restrictions. To date the Company has made no draw downs under the 2007 CEFF.

***Warrants***

In connection with its building lease, the Company issued warrants to purchase 100,000 shares of common stock for \$0.58 per share in July 1999. The fair value of the warrants, calculated using the Black-Scholes pricing model, was capitalized in other assets and amortized over the life of the building lease, which expired in August 2000. The amount charged to rent expense was \$11,000 from August 5, 1997 (date of inception) through August 2000. The warrants were fully exercised in 2004 in a cashless exercise.

The Company has issued warrants to purchase convertible preferred stock, which became exercisable for common stock upon the conversion of the outstanding shares of preferred stock into common stock in conjunction with the Company's initial public offering. In September 1998, in connection with an equipment line of credit financing, the Company issued warrants to the lender. The Company valued the warrants by using the Black-Scholes pricing model in fiscal 1999 when the line was drawn, and the fair value of \$30,000 was recorded as a discount to the debt and amortized to interest expense over the life of the equipment line. In August 2005, these warrants were exercised by the lender in a cashless exercise, yielding 13,199 shares of common stock on a net basis. In connection with a convertible preferred stock financing in August 1999, the Company issued warrants to the preferred stockholders. The warrants were valued at \$467,000 using the Black-Scholes pricing model and the value was recorded as issuance cost as an offset to convertible preferred stock. These warrants expired unexercised on August 30, 2006. In connection with an equipment line of credit, the Company issued warrants to the lender in December 1999. The value of the warrants was calculated using the Black-Scholes pricing model and was deemed insignificant. In August 2005, these warrants were exercised by the lender in a cashless exercise, yielding 1,333 shares of common stock on a net basis.

The Company issued warrants to purchase 244,000 of common stock to Kingsbridge in connection with the CEFF that was entered into in October 2005. The warrants are exercisable at a price of \$9.13 per share beginning six months after the date of grant and for a period of five years thereafter. The warrants were valued at \$920,000 using the Black-Scholes pricing model and the following assumptions: a contractual term of five years, risk-free interest rate of 4.3%, volatility of 67%, and the fair value of our stock price on the date of performance commitment, October 28, 2005, of \$7.02. The warrant value was recorded as an issuance cost in additional paid-in capital on the initial draw down of the CEFF in December 2005. These warrants are vested and fully exercisable as of December 31, 2007.

The Company issued warrants to purchase 230,000 shares of common stock to Kingsbridge in connection with the 2007 CEFF. The warrants are exercisable at a price of \$7.99 per share beginning six months after the date of grant and

for a period of three years thereafter. The warrants were valued at \$594,000 using the Black-Scholes pricing model and the following assumptions: a contractual term of three years, risk-free interest rate of 4.275%, volatility of 73%, and the fair value of the Company's stock price on the date of performance commitment, October 15, 2007, of \$6.00. The warrant value will be recorded as an issuance cost in additional paid-in capital on

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the initial draw down of the 2007 CEFF. These warrants are vested and fully exercisable as of December 31, 2007. To date the Company has made no drawdowns under the 2007 CEFF.

Outstanding warrants were as follows at December 31, 2007:

| <b>Number<br/>of Shares</b> | <b>Exercise<br/>Price</b> | <b>Expiration<br/>Date</b> |
|-----------------------------|---------------------------|----------------------------|
| 244,000                     | \$ 9.13                   | 04/28/11                   |
| 230,000                     | \$ 7.99                   | 04/15/11                   |

***Stock Option Plans******2004 Plan***

In January 2004, the Board of Directors adopted the 2004 Equity Incentive Plan (the 2004 Plan), which was approved by the stockholders in February 2004. The 2004 Plan provides for the granting of incentive stock options, nonstatutory stock options, restricted stock purchase rights and stock bonuses to employees, directors and consultants. Under the 2004 Plan, options may be granted at prices not lower than 85% and 100% of the fair market value of the common stock on the date of grant for nonstatutory stock options and incentive stock options, respectively. Options granted to new employees generally vest 25% after one year and monthly thereafter over a period of four years. Options granted to existing employees generally vest monthly over a period of four years. As of December 31, 2007, 1,497,296 shares of common stock were authorized for issuance under the 2004 Plan. On January 1, 2008 and annually thereafter through January 2009, the number of authorized shares automatically increases by a number of shares equal to the lesser of (i) 1,500,000 shares, (ii) 3.5% of the outstanding shares on such date, or (iii) an amount determined by the Board of Directors. Accordingly, on January 1, 2008, the number of shares of common stock authorized for issuance under the 2004 Plan was increased to a total of 2,997,296 shares.

***1997 Plan***

In 1997, the Company adopted the 1997 Stock Option/Stock Issuance Plan (the 1997 Plan). The Plan provides for the granting of stock options to employees and consultants of the Company. Options granted under the 1997 Plan may be either incentive stock options or nonstatutory stock options. Incentive stock options may be granted only to Company employees (including officers and directors who are also employees). Nonstatutory stock options may be granted to Company employees and consultants. Options under the Plan may be granted for terms of up to ten years from the date of grant as determined by the Board of Directors, provided, however, that (i) the exercise price of an incentive stock option and nonstatutory shall not be less than 100% and 85% of the estimated fair market value of the shares on the date of grant, respectively, and (ii) with respect to any 10% shareholder, the exercise price of an incentive stock option or nonstatutory stock option shall not be less than 110% of the estimated fair market value of the shares on the date of grant and the term of the grant shall not exceed five years. Options may be exercisable immediately and are subject to repurchase options held by the Company which lapse over a maximum period of ten years at such times and under such conditions as determined by the Board of Directors. To date, options granted generally vest over four or

five years (generally 25% after one year and monthly thereafter). As of December 31, 2007, the Company had reserved 1,246,215 shares of common stock for issuance related to options outstanding under the 1997 Plan, and there were no shares available for future grants under the 1997 Plan.

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Activity under the two stock option plans was as follows:

|                               | <b>Options<br/>Available for<br/>Grant</b> | <b>Options<br/>Outstanding</b> | <b>Weighted<br/>Average<br/>Exercise<br/>Price per Share</b> |
|-------------------------------|--|--------------------------------|--|
| Options authorized            | 1,000,000                                  |                                | \$   |
| Options granted               | (833,194)                                  | 833,194                        | 0.20   |
| Options exercised             |  | (147,625)                      | 0.015  |
| Options forfeited             |  |                                |  |
| Balance at December 31, 1998  | 166,806                                    | 685,569                        | 0.12   |
| Increase in authorized shares | 461,945                                    |                                |  |
| Options granted               | (582,750)                                  | 582,750                        | 0.39   |
| Options exercised             |  | (287,500)                      | 0.24   |
| Options forfeited             | 50,625                                     | (50,625)                       | 0.20   |
| Balance at December 31, 1999  | 96,626                                     | 930,194                        | 0.25   |
| Increase in authorized shares | 1,704,227                                  |                                |  |
| Options granted               | (967,500)                                  | 967,500                        | 0.58   |
| Options exercised             |  | (731,661)                      | 0.27   |
| Options forfeited             | 68,845                                     | (68,845)                       | 0.30   |
| Balance at December 31, 2000  | 902,198                                    | 1,097,188                      | 0.52   |
| Options granted               | (525,954)                                  | 525,954                        | 1.12   |
| Options exercised             |  | (102,480)                      | 0.55   |
| Options forfeited             | 109,158                                    | (109,158)                      | 0.67   |
| Balance at December 31, 2001  | 485,402                                    | 1,411,504                      | 0.73   |
| Increase in authorized shares | 1,250,000                                  |                                |  |
| Options granted               | (932,612)                                  | 932,612                        | 1.20   |
| Options exercised             |  | (131,189)                      | 0.64   |
| Options forfeited             | 152,326                                    | (152,326)                      | 0.78   |
| Balance at December 31, 2002  | 955,116                                    | 2,060,601                      | 0.95   |
| Options granted               | (613,764)                                  | 613,764                        | 1.39   |
| Options exercised             |  | (380,662)                      | 1.02   |
| Options forfeited             | 49,325                                     | (49,325)                       | 0.89   |
| Balance at December 31, 2003  | 390,677                                    | 2,244,378                      | 1.06   |
| Increase in authorized shares | 1,600,000                                  |                                |  |

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|                               |             |           |      |
|-------------------------------|-------------|-----------|------|
| Options granted               | (863,460)   | 863,460   | 7.52 |
| Options exercised             |             | (404,618) | 1.12 |
| Options forfeited             | 74,025      | (58,441)  | 3.64 |
| Options retired               | (36,128)    |           |      |
| Balance at December 31, 2004  | 1,165,114   | 2,644,779 | 3.10 |
| Increase in authorized shares | 995,861     |           |      |
| Options granted               | (996,115)   | 996,115   | 7.23 |
| Options exercised             |             | (196,703) | 1.48 |
| Options forfeited             | 182,567     | (161,958) | 5.89 |
| Balance at December 31, 2005  | 1,347,427   | 3,282,233 | 4.31 |
| Increase in authorized shares | 1,039,881   |           |      |
| Options granted               | (1,250,286) | 1,250,286 | 7.04 |
| Options exercised             |             | (354,502) | 1.47 |
| Options forfeited             | 146,854     | (145,317) | 7.16 |
| Balance at December 31, 2006  | 1,283,876   | 4,032,700 | 5.31 |
| Increase in authorized shares | 1,500,000   |           |      |
| Options granted               | (1,647,570) | 1,647,570 | 6.65 |
| Options exercised             |             | (259,054) | 1.95 |
| Options forfeited             | 360,990     | (360,922) | 6.94 |
| Balance at December 31, 2007  | 1,497,296   | 5,060,294 | 5.80 |

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**NOTES TO FINANCIAL STATEMENTS (Continued)**

The options outstanding and currently exercisable by exercise price at December 31, 2007 were as follows:

| Range of Exercise Price | Number of Options | Options Outstanding             |   | Vested and Exercisable |                                 |
|-------------------------|-------------------|---------------------------------|---|------------------------|---------------------------------|
|                         |                   | Weighted Average Exercise Price | Weighted Average Remaining Contractual Life (Years) | Number of Options      | Weighted Average Exercise Price |
| \$0.20 - \$1.00         | 319,265           | \$ 0.55                         | 2.47  | 319,265                | \$ 0.55                         |
| \$1.20                  | 671,474           | \$ 1.20                         | 4.76  | 671,474                | \$ 1.20                         |
| \$2.00 - \$5.00         | 209,594           | \$ 3.50                         | 7.92  | 74,490                 | \$ 2.07                         |
| \$5.01 - \$6.78         | 815,373           | \$ 6.38                         | 7.25  | 580,113                | \$ 6.45                         |
| \$6.81                  | 1,167,936         | \$ 6.81                         | 9.16  | 221,490                | \$ 6.81                         |
| \$6.82 - \$7.04         | 531,528           | \$ 7.01                         | 8.11  | 217,788                | \$ 7.01                         |
| \$7.10                  | 269,737           | \$ 7.10                         | 6.91  | 188,141                | \$ 7.10                         |
| \$7.15                  | 513,400           | \$ 7.15                         | 8.16  | 224,683                | \$ 7.15                         |
| \$7.17 - \$9.95         | 549,487           | \$ 9.09                         | 7.21  | 389,720                | \$ 9.22                         |
| \$10.12 - \$15.95       | 12,500            | \$ 12.45                        | 6.55  | 10,676                 | \$ 12.62                        |
|                         | 5,060,294         | \$ 5.80                         | 7.25  | 2,897,840              | \$ 5.03                         |

The weighted-average grant-date fair value of options granted during the year ended December 31, 2007 was \$4.50 per share. The total intrinsic value of options exercised during the year ended December 31, 2007 was \$1.0 million. The aggregate intrinsic value of options outstanding and options exercisable as of December 31, 2007 was \$4.0 million and \$3.9 million, respectively. The intrinsic value is calculated as the difference between the market value as of December 31, 2007 and the exercise price of shares. The market value as of December 31, 2007 was \$4.73 as reported by NASDAQ. As of December 31, 2007 the total number of options vested and expected to vest was 4,926,569 with a weighted average exercise price of \$5.77 per share, aggregate intrinsic value of \$4.0 million and weighted average remaining contractual life of 7.20 years.

As of December 31, 2006, there were 2,240,233 options outstanding, exercisable and vested at a weighted average exercise price of \$4.00 per share. As of December 31, 2005, there were 2,190,664 options outstanding, exercisable and vested at a weighted average exercise price of \$2.58 per share. The weighted average grant date fair value of options granted in the years ended December 31, 2006 and 2005 was \$4.88 and \$4.76, respectively.

**Stock-based Compensation**

*Deferred Employee Stock-Based Compensation*

In anticipation of the Company's 2004 initial public offering, the Company determined that, for financial reporting purposes, the estimated value of its common stock was in excess of the exercise prices of its stock options. Accordingly, for stock options issued to employees prior to its IPO, the Company recorded deferred stock-based compensation and is amortizing the related expense on a straight line basis over the service period, which is generally four years. The Company recorded deferred employee stock compensation of \$6.2 million for the period from August 5, 1997 (date of inception) through December 31, 2007. For the years ended December 31, 2007 and 2006, the Company recorded no deferred stock compensation. For the years ended December 31, 2007, 2006 and 2005, the Company recorded amortization of deferred stock-based compensation of \$0.7 million, \$1.2 million, and \$1.3 million, respectively, in connection with options granted to employees.

*Non-employee Stock-Based Compensation*

Stock-based compensation expense related to stock options granted to non-employees is recognized as the stock options are earned. The Company believes that the fair value of the stock options is more reliably measurable than the fair value of the services received. The fair value of the stock options granted is calculated at each reporting



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**NOTES TO FINANCIAL STATEMENTS (Continued)**

date using the Black-Scholes option-pricing model as prescribed by SFAS No. 123R using the following assumptions:

|                             | <b>Years Ended December 31,</b> |             |             |
|-----------------------------|---------------------------------|-------------|-------------|
|                             | <b>2007</b>                     | <b>2006</b> | <b>2005</b> |
| Risk-free interest rate     | 4.72%                           | 4.88%       | 4.27%       |
| Volatility                  | 74%                             | 72%         | 77%         |
| Contractual life (in years) | 10.0                            | 10.0        | 10.0        |
| Expected dividend yield     | 0.00%                           | 0.00%       | 0.00%       |

There were no options granted to non-employees for the years ended December 31, 2007, 2006 or 2005.

In connection with the grant of stock options to non-employees, the Company recorded stock-based compensation expense of \$14,000, \$27,000, and \$78,000 in 2007, 2006, and 2005, respectively, and \$1.3 million for the period from August 5, 1997 (date of inception) through December 31, 2007.

***Employee Stock Purchase Plan***

In January 2004, the Board of Directors adopted the ESPP, which was approved by the stockholders in February 2004. Under the ESPP, statutory employees may purchase common stock of the Company up to a specified maximum amount through payroll deductions. The stock is purchased semi-annually at a price equal to 85% of the fair market value at certain plan-defined dates. We issued 179,835, 193,248, and 179,520 shares of common stock during 2007, 2006, and 2005, respectively, pursuant to the ESPP at an average price of \$4.49 per share, \$4.43 per share, and \$4.25 per share in 2007, 2006, and 2005, respectively. At December 31, 2007 the Company had 877,998 shares of common stock reserved for issuance under the ESPP.

**Note 11 Income Taxes**

The Company did not record an income tax provision in the years ended December 31, 2007, 2006 and 2005 because the Company had a net taxable loss in each of those periods.

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The significant components of the Company's deferred tax assets and liabilities were as follows (in thousands):

|                               | <b>As of December 31,</b> |             |
|-------------------------------|---------------------------|-------------|
|                               | <b>2007</b>               | <b>2006</b> |
| Deferred tax assets:          |                           |             |
| Depreciation and amortization | \$ 10,213                 | \$ 8,121    |
| Reserves and accruals         | 973                       | 248         |

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|                           |           |           |
|---------------------------|-----------|-----------|
| Net operating losses      | 95,706    | 80,636    |
| Tax credits               | 13,761    | 13,309    |
| Total deferred tax assets | 120,653   | 102,314   |
| Less: Valuation allowance | (120,653) | (102,314) |
| Net deferred tax assets   | \$        | \$        |

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**NOTES TO FINANCIAL STATEMENTS (Continued)**

Following is a reconciliation of the statutory federal income tax rate to the Company's effective tax rate:

|   | <b>For The Years Ended</b> |              |              |
|---|----------------------------|--------------|--------------|
|   | <b>December 31,</b>        |              |              |
|   | <b>2007</b>                | <b>2006</b>  | <b>2005</b>  |
| Tax at federal statutory tax rate   | (34)%                      | (34)%        | (34)%        |
| State income tax, net of federal tax benefit  | (6)%                       | (6)%         | (6)%         |
| Research and development credits  | (5)%                       | (5)%         | (4)%         |
| Adjustment to prior year research and development credits due to results of research and development credit study | 2%                         |              |              |
| Adjustment due to Section 383 limitation  | 2%                         |              |              |
| Deferred tax assets not benefited   | 38%                        | 43%          | 44%          |
| Stock based compensation  | 3%                         | 2%           | 0%           |
| Permanent items   | 0%                         | 0%           | 0%           |
| <b>Total</b>  | <b>\$ 0%</b>               | <b>\$ 0%</b> | <b>\$ 0%</b> |

Management believes that, based upon a number of factors, it is more likely than not that the deferred tax assets will not be realized; therefore a full valuation allowance has been recorded. The valuation allowance increased by \$18.3 million in 2007, \$26.1 million in 2006 and \$17.9 million in 2005.

The Company had federal net operating loss carryforwards of approximately \$265.2 million and state net operating loss carryforwards of approximately \$95.1 million at December 31, 2007. The federal and state operating loss carryforwards will begin to expire in 2018 and 2008, respectively, if not utilized. The net operating loss carryforwards include deductions for stock options. When utilized, the portion related to stock options deductions will be accounted for as a credit to stockholders' equity rather than as a reduction of the income tax provision.

The Company had research credit carryforwards of approximately \$7.5 million and \$9.1 million for federal and state income tax purposes, respectively, at December 31, 2007. If not utilized, the federal carryforwards will expire in various amounts beginning in 2018. The California state credit can be carried forward indefinitely.

The Tax Reform Act of 1986 limits the use of net operating loss and tax credit carryforwards in certain situations where equity transactions resulted in a change of ownership as defined by Internal Revenue Code Section 382. During the year ended December 31, 2007, the Company conducted a study and determined that the Company's use of its federal research credit is subject to such a restriction. Accordingly, the Company reduced its deferred tax assets and the corresponding valuation allowance by \$0.8 million. As a result, the research credit amount as of December 31, 2007 reflects the restriction on the Company's ability to use the credit.

In July 2006, the FASB issued FIN 48 which prescribes a comprehensive model for how companies should recognize, measure, present, and disclose in their financial statements uncertain tax positions taken or expected to be taken on a

tax return. Under FIN 48, tax positions must initially be recognized in the financial statements when it is more likely than not the position will be sustained upon examination by the tax authorities. Such tax positions must initially and subsequently be measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon ultimate settlement with the tax authority assuming full knowledge of the position and relevant facts. FIN 48 is effective for fiscal years beginning after December 15, 2006.

This statement became effective for the Company on January 1, 2007. The cumulative effect of adopting FIN 48 on January 1, 2007 resulted in no FIN 48 liability on the balance sheet. The total amount of unrecognized tax benefits as of the date of adoption was \$3.1 million. The Company is currently not subject to income tax examinations and, in general, all tax years remain open due to net operating losses.

Interest and penalties are zero, and the Company's policy to account for interest and penalties is to classify both as income tax expense in the financial statements. Because the Company has recorded a full valuation allowance on

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all its deferred tax assets, FIN 48 has had no impact on the Company's effective tax rate. The Company does not expect its unrecognized tax benefits to change materially over the next 12 months.

The following is a tabular reconciliation of the total amounts of unrecognized tax benefits ( UTB s ) for the year ended December 31, 2007 (in thousands):

|  | <b>Federal<br/>and State<br/>Tax</b> | <b>Federal Tax<br/>Benefit<br/>of State Income<br/>Tax<br/>UTBs</b> |    | <b>Unrecognized Income<br/>Tax<br/>Benefits- Net of<br/>Federal<br/>Benefit of State UTB s</b> |
|--|--------------------------------------|---|----|--|
| Unrecognized tax benefits balance at January 1, 2007   | \$ 3,129                             | \$ 566  | \$ | 2,563  |
| Reduction for tax positions of prior years             | (232)                                | 96  |    | (328)  |
| Addition for tax positions related to the current year | 644                                  | 130   |    | 514  |
| Unrecognized tax benefits balance at December 31, 2007 | \$ 3,541                             | \$ 792  | \$ | 2,749  |

**Note 12 Quarterly Financial Data (Unaudited)**

Quarterly results were as follows (in thousands, except per share data):

|                                      | <b>First<br/>Quarter</b> | <b>Second<br/>Quarter</b> | <b>Third<br/>Quarter</b> | <b>Fourth<br/>Quarter</b> |
|--------------------------------------|--------------------------|---------------------------|--------------------------|---------------------------|
| <b>2007</b>                          |                          |                           |                          |                           |
| Total revenues                       | \$ 3,205                 | \$ 3,177                  | \$ 4,130                 | \$ 3,109                  |
| Net loss                             | (11,692)                 | (12,628)                  | (11,321)                 | (13,253)                  |
| Net loss per share basic and diluted | \$ (0.25)                | \$ (0.27)                 | \$ (0.24)                | \$ (0.27)                 |
| <b>2006</b>                          |                          |                           |                          |                           |
| Total revenues                       | \$ 1,420                 | \$ 1,446                  | \$ 106                   | \$ 156                    |
| Net loss                             | (12,464)                 | (13,786)                  | (14,920)                 | (15,946)                  |
| Net loss per share basic and diluted | \$ (0.36)                | \$ (0.38)                 | \$ (0.41)                | \$ (0.41)                 |

**Note 13 Subsequent Events**

In January 2008, GE Capital approved a reduction in the amount of our certificate of deposit of \$1.0 million (See Note 7 Equipment Financing Line and Note 1 Organization and Summary of Significant Accounting Policies *Restricted Cash* .)

In February 2008, the Company's consulting agreement with Dr. Homcy was amended effective retroactively as of November 1, 2007. The amended agreement sets forth the consulting services Dr. Homcy will perform and provides for a minimum annual consulting fee of \$15,000 for such services, payable quarterly in arrears. The amended agreement is effective through December 31, 2008, but also provides for automatic renewals of the agreement for successive one-year terms. Either party may terminate the consulting agreement on sixty days notice.

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**NOTES TO FINANCIAL STATEMENTS (Continued)**

In January 2008, the Company's auction rate securities with January auction reset dates had successful auctions at which their interest rates were reset. In February 2008, the Company liquidated \$3.2 million of its auction rate securities at par, which were classified as short-term investments as of December 31, 2007. As of March 4, 2008, \$20.0 million of auction rate securities remained in the Company's portfolio and auctions for these securities failed in February and early March 2008. As a result of this development and the remaining uncertainty in the market for auction rate securities, the Company has classified \$20.0 million of auction rate securities as long-term in the accompanying balance sheet as of December 31, 2007. These failures resulted in the interest rates on these investments resetting to contractually stipulated fail rates that are variable based on short-term municipal bond or other market indices, or fixed rates that may result in the Company earning above-market interest rates on these investments. If the Company needs to access these funds, it will not be able to do so until a future auction on these investments is successful, the issuer redeems the outstanding securities, the securities mature, or the Company sells the securities in the secondary market.

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**Item 9. *Changes in and Disagreements With Accountants on Accounting and Financial Disclosure***

None.

**Item 9A. *Controls and Procedures***

*Evaluation of disclosure controls and procedures.* Our management evaluated, with the participation of our Chief Executive Officer and our Chief Financial Officer, the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that the Company's disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to management as appropriate to allow timely decisions regarding required disclosures.

*Management's Report on Internal Control over Financial Reporting.* Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2007. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework. Our management has concluded that, as of December 31, 2007, our internal control over financial reporting is effective based on these criteria.

Our independent registered public accounting firm, PricewaterhouseCoopers LLP, has audited the effectiveness of our internal control over financial reporting as of December 31, 2007, as stated in their report, which is included herein.

*Changes in internal control over financial reporting.* There was no change in our internal control over financial reporting that occurred during the quarter ended December 31, 2007 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. *Other Information***

None.

**PART III**

**Item 10. *Directors, Executive Officers and Corporate Governance***

The information regarding our directors and executive officers, our director nominating process and our audit committee is incorporated by reference from our definitive Proxy Statement for our 2008 Annual Meeting of Stockholders, where it appears under the headings Board of Directors and Executive Officers.

**Section 16(a) Beneficial Ownership Reporting Compliance**

The information regarding our Section 16 beneficial ownership reporting compliance is incorporated by reference from our definitive Proxy Statement described above, where it appears under the headings Section 16(a) Beneficial Ownership Reporting Compliance.

**Code of Ethics**



We have adopted a Code of Ethics that applies to all directors, officers and employees of the Company. We publicize the Code of Ethics through posting the policy on our website, <http://www.cytokinetics.com>. We will disclose on our website any waivers of, or amendments to, our Code of Ethics.

**Item 11. *Executive Compensation***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above, where it appears under the headings Executive Compensation and Compensation Committee Interlocks and Insider Participation.

**Table of Contents****Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required by this Item regarding security ownership of certain beneficial owners and management is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above, where it appears under the heading Security Ownership of Certain Beneficial Owners and Management.

The following table summarizes the securities authorized for issuance under our equity compensation plans as of December 31, 2007:

| <b>Plan Category</b>                                   | <b>Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights</b> | <b>Weighted Average Exercise Price of Outstanding Options, Warrants and Rights</b> | <b>Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans(1)</b> |
|--|--|--|--|
| Equity compensation plans approved by stockholders     | 5,060,294  | \$ 5.80  | 1,497,296  |
| Equity compensation plans not approved by stockholders |  |  |  |
| <b>Total</b>   | <b>5,060,294</b>   | <b>\$ 5.80</b>   | <b>1,497,296</b>   |

(1) The number of authorized shares automatically increases annually by a number of shares equal to the lesser of (i) 1,500,000 shares, (ii) 3.5% of the outstanding shares on such date, or (iii) an amount determined by the Board of Directors. On January 1, 2008, the number of shares of stock available for future issuance under our 2004 Equity Incentive Plan was automatically increased by 1,500,000 to 2,997,296 pursuant to the terms of the plan.

**Item 13. Certain Relationships and Related Transactions, and Director Independence**

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the headings Certain Business Relationships and Related Party Transactions and Board of Directors.

**Item 14. Principal Accounting Fees and Services**

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above, where it appears under the heading Principal Accountant Fees and Services.

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**PART IV**

**Item 15. Exhibits and Financial Statement Schedules**

(a) The following documents are filed as part of this Form 10-K:

(1) Financial Statements (included in Part II of this report):

Report of Independent Registered Public Accounting Firm

Balance Sheets

Statements of Operations

Statements of Stockholders' Equity (Deficit)

Statements of Cash Flows

Notes to Financial Statements

(2) Financial Statement Schedules:

None All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

(3) Exhibits:

| <b>Exhibit Number</b> | <b>Description</b>  |
|-----------------------|---|
| 3.1                   | Amended and Restated Certificate of Incorporation.(1)   |
| 3.2                   | Amended and Restated Bylaws.(1)   |
| 4.1                   | Specimen Common Stock Certificate.(20)  |
| 4.2                   | Fourth Amended and Restated Investors Rights Agreement, dated March 21, 2003, by and among the Company and certain stockholders of the Registrant.(1) |
| 4.3                   | Master Security Agreement, dated February 2, 2001, by and between the Company and General Electric Capital Corporation.(1)                            |
| 4.4                   | Cross-Collateral and Cross-Default Agreement by and between the Company and General Electric Capital Corporation.(1)                                  |
| 4.5                   | Warrant for the purchase of shares of common stock, dated July 20, 1999, issued by the Company to Bristow Investments, L.P.(1)                        |
| 4.6                   | Warrant for the purchase of shares of common stock, dated July 20, 1999, issued by the Company to the Laurence and Magdalena Shushan Family Trust.(1) |
| 4.7                   | Warrant for the purchase of shares of common stock, dated July 20, 1999, issued by the Company to Slough Estates USA Inc.(1)                          |
| 4.9                   |   |

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- Warrant for the purchase of shares of common stock, dated October 28, 2005, issued by the Company to Kingsbridge Capital Limited.(9)
- 4.10 Registration Rights Agreement, dated October 28, 2005, by and between the Company and Kingsbridge Capital Limited.(9)
- 4.11 Registration Rights Agreement, dated as of December 29, 2006, by and between the Company and Amgen Inc.(16)
- 4.12 Warrant for the purchase of shares of common stock, dated October 15, 2007, issued by the Company to Kingsbridge Capital Limited.(19)
- 4.13 Registration Rights Agreement, dated October 15, 2007, by and between the Company and Kingsbridge Capital Limited.(19)
- 10.1 Form of Indemnification Agreement between the Company and each of its directors and officers.(1)
- 10.2 1997 Stock Option/Stock Issuance Plan.(1)
- 10.3 2004 Equity Incentive Plan.(1)
- 10.4 2004 Employee Stock Purchase Plan.(1)
- 10.5 Build-to-Suit Lease, dated May 27, 1997, by and between Britannia Pointe Grand Limited Partnership and Metaxen, LLC.(1)

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| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| 10.6                      | First Amendment to Lease, dated April 13, 1998, by and between Britannia Pointe Grand Limited Partnership and Metaxen, LLC.(1)  |
| 10.7                      | Sublease Agreement, dated May 1, 1998, by and between the Company and Metaxen LLC.(1)   |
| 10.8                      | Sublease Agreement, dated March 1, 1999, by and between Metaxen, LLC and Exelixis Pharmaceuticals, Inc.(1)  |
| 10.9                      | Assignment and Assumption Agreement and Consent, dated July 11, 1999, by and among Exelixis Pharmaceuticals, Metaxen, LLC, Xenova Group PLC and Britannia Pointe Grande Limited Partnership.(1) |
| 10.10                     | Second Amendment to Lease, dated July 11, 1999, by and between Britannia Pointe Grand Limited Partnership and Exelixis Pharmaceuticals, Inc.(1)   |
| 10.11                     | First Amendment to Sublease Agreement, dated July 20, 1999, by and between the Company and Metaxen.(1)  |
| 10.12                     | Agreement and Consent, dated July 20, 1999, by and among Exelixis Pharmaceuticals, Inc., the Company and Britannia Pointe Grand Limited Partnership.(1)   |
| 10.13                     | Amendment to Agreement and Consent, dated July 31, 2000, by and between the Company, Exelixis, Inc., and Britannia Pointe Grande Limited Partnership.(1)  |
| 10.14                     | Assignment and Assumption of Lease, dated September 28, 2000, by and between Exelixis, Inc. and the Company.(1)   |
| 10.15                     | Sublease Agreement, dated September 28, 2000, by and between the Company and Exelixis, Inc.(1)  |
| 10.16                     | Sublease Agreement, dated December 29, 1999, by and between the Company and COR Therapeutics, Inc.(1)   |
| *10.17                    | Collaboration and License Agreement, dated June 20, 2001, by and between the Company and Glaxo Group Limited.(1)  |
| *10.18                    | Memorandum, dated June 20, 2001, by and between the Company and Glaxo Group Limited.(1)   |
| *10.19                    | Letter Amendment to Collaboration Agreement, dated October 28, 2002, by and between the Company and Glaxo Group Limited.(1)   |
| *10.20                    | Letter Amendment to Collaboration Agreement, dated November 5, 2002, by and between the Company and Glaxo Group Limited.(1)   |
| *10.21                    | Letter Amendment to Collaboration Agreement, dated December 13, 2002, by and between the Company and Glaxo Group Limited.(1)  |
| *10.22                    | Letter Amendment to Collaboration Agreement, dated July 11, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| *10.23                    | Letter Amendment to Collaboration Agreement, dated July 28, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| *10.24                    | Letter Amendment to Collaboration Agreement, dated July 28, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| *10.25                    | Letter Amendment to Collaboration Agreement, dated July 28, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| 10.26                     | Series D Preferred Stock Purchase Agreement, dated June 20, 2001, by and between the Company and Glaxo Wellcome International B.V.(1)   |
| 10.27                     | Amendment No. 1 to Series D Preferred Stock Purchase Agreement, dated April 2, 2003, by and among the Company, Glaxo Wellcome International B.V. and Glaxo Group Limited.(1)                    |
| *10.28                    | Exclusive License Agreement between The Board of Trustees of the Leland Stanford Junior University, The Regents of the University of California, and the Company dated April 21, 1998.(1)       |
| 10.29                     |   |

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Modification Agreement between The Regents of the University of California, The Board of Trustees of the Leland Stanford Junior University and the Company, dated September 1, 2000.(1)

\*10.30 Collaboration and License Agreement, dated December 15, 2003, by and between AstraZeneca AB and the Company.(1)

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| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| 10.31                     | David J. Morgans and Sandra Morgans Promissory Note, dated May 20, 2002.(1)   |
| 10.32                     | David J. Morgans and Sandra Morgans Promissory Note, dated October 18, 2000.(1)   |
| 10.33                     | James H. Sabry and Sandra J. Spence Promissory Note, dated November 12, 2001.(1)  |
| 10.34                     | Robert I. Blum Cash Bonus Agreement, dated September 1, 2002.(1)  |
| 10.35                     | Robert I. Blum Amended and Restated Cash Bonus Agreement, dated December 1, 2003.(1)  |
| 10.36                     | David J. Morgans Cash Bonus Agreement, dated September 1, 2002.(1)  |
| 10.37                     | David J. Morgans Amended and Restated Cash Bonus Agreement, dated December 1, 2003.(1)  |
| 10.38                     | Jay K. Trautman Cash Bonus Agreement, dated September 1, 2002.(1)   |
| 10.39                     | Jay K. Trautman Amended and Restated Cash Bonus Agreement, dated December 1, 2003.(1)   |
| 10.40                     | Common Stock Purchase Agreement, dated March 10, 2004, by and between the Company and Glaxo Group Limited.(1)   |
| *10.41                    | Collaboration and Facilities Agreement, dated August 19, 2004, by and between the Company and Portola Pharmaceuticals, Inc.(2)  |
| 10.42                     | Executive Employment Agreement, dated July 8, 2004, by and between the Company and Jay Trautman.(2)   |
| 10.43                     | Executive Employment Agreement, dated July 14, 2004, by and between the Company and James Sabry.(2)   |
| 10.44                     | Executive Employment Agreement, dated July 14, 2004, by and between the Company and David Morgans.(2)   |
| 10.45                     | Executive Employment Agreement, dated September 1, 2004, by and between the Company and Robert Blum.(2)   |
| 10.46                     | Executive Employment Agreement, dated September 7, 2004, by and between the Company and Sharon Surrey-Barbari.(2)   |
| 10.47                     | Executive Employment Agreement, dated as of August 22, 2005, by and between the Company and Andrew Wolff.(7)  |
| 10.48                     | Executive Employment Agreement, dated February 1, 2005, by and between the Company and David Cragg.(10)   |
| *10.49                    | First Amendment to Collaboration and Facilities Agreement, dated March 24, 2005, by and between the Company and Portola Pharmaceuticals, Inc.(3)                      |
| *10.50                    | Amendment to the Collaboration and License Agreement with GlaxoSmithKline, effective as of September 21, 2005, by and between the Company and Glaxo Group Limited.(5) |
| 10.51                     | Sublease, dated as of November 29, 2005, by and between the Company and Millennium Pharmaceuticals, Inc.(6)   |
| 10.52                     | Common Stock Purchase Agreement, dated as of October 28, 2005, by and between the Company and Kingsbridge Capital Limited.(9)   |
| 10.53                     | Stock Purchase Agreement dated January 18, 2006, by and among the Company, Federated Kaufmann Fund and Red Abbey Venture Partners, LLC.(8)                            |
| 10.54                     | Letter Agreement dated January 17, 2006, by and between the Company and Pacific Growth Equities LLC.(8)   |
| 10.55                     | GE Loan Proposal, dated as of January 18, 2006, by and between the Company and GE.(9)   |
| 10.56                     | GE Loan Proposal, executed as of March 16, 2006, by and between the Company and General Electric Capital Corporation.(11)   |
| *10.57                    | Second Amendment to Collaboration and Facilities Agreement, dated March 17, 2006, by and between the Company and Portola Pharmaceuticals, Inc.(11)                    |
| *10.58                    |   |

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Letter Amendment to the Collaboration Agreement, dated June 16, 2006, by and between the Company and Glaxo Group Limited.(12)

10.59 Sublease Agreement, dated August 4, 2006, by and between the Company and Portola Pharmaceuticals, Inc.(13)



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| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| *10.60                    | Amendment to the Collaboration and License Agreement, dated November 27, 2006, by and between the Company and Glaxo Group Limited.(14)                                    |
| 10.61                     | Common Stock Purchase Agreement, dated as of December 29, 2006, by and between the Company and Amgen Inc.(15)   |
| *10.62                    | Collaboration and Option Agreement, dated as of December 29, 2006, by and between the Company and Amgen Inc.(20)  |
| *10.63                    | Letter Amendment to the Collaboration and License Agreement, dated June 18, 2007, by and between the Company and Glaxo Group Limited, a GlaxoSmithKline company.(16)      |
| 10.64                     | GE Loan Proposal, executed as of August 28, 2007, by and between the Company and General Electric Capital Corporation.(17)  |
| 10.65                     | Common Stock Purchase Agreement, dated as of October 15, 2007, by and between the Company and Kingsbridge Capital Limited.(18)  |
| 23.1                      | Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.   |
| 24.1                      | Power of Attorney (see page 113)  |
| 31.1                      | Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.   |
| 31.2                      | Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.   |
| 32.1                      | Certifications of the Principal Executive Officer and the Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. Section 1350). |

- (1) Incorporated by reference from our registration statement on Form S-1, registration number 333-112261, declared effective by the Securities and Exchange Commission on April 29, 2004.
- (2) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on November 12, 2004, as amended February 16, 2005.
- (3) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on May 12, 2005.
- (4) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on August 12, 2005.
- (5) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on November 10, 2005.
- (6) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 5, 2005, as amended on December 13.
- (7) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 12, 2005.
- (8) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on January 18, 2006.
- (9)

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Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on January 20, 2006.

- (10) Incorporated by reference from our Annual Report on Form 10-K, filed with the Securities and Exchange Commission on March 10, 2006.
- (11) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on March 22, 2006.
- (12) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 19, 2006.
- (13) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on August 8, 2006.
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- (15) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on January 3, 2007.
- (16) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 19, 2007.
- (17) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 29, 2007.
- (18) Incorporated by reference from our Current Report on Form 8-K, filed with the Securities and Exchange Commission on October 15, 2007.
- (19) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on May 9, 2007.
- (20) Incorporated by reference from our Annual Report on Form 10-K, filed with the Securities and Exchange Commission on March 12, 2007.

\* Pursuant to a request for confidential treatment, portions of this Exhibit have been redacted from the publicly filed document and have been furnished separately to the Securities and Exchange Commission as required by Rule 406 under the Securities Act of 1933 or Rule 24b-2 under the Securities Exchange Act of 1934, as applicable.

(b) Exhibits

The exhibits listed under Item 14(a)(3) hereof are filed as part of this Form 10-K other than Exhibit 32.1 which shall be deemed furnished.

(c) Financial Statement Schedules

All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

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**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities and Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CYTOKINETICS, INCORPORATED

By: /s/ Robert I. Blum

Robert I. Blum  
President, Chief Executive Officer and Director

Dated: March 12, 2008

**POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Robert I. Blum and Sharon Surrey-Barbari, and each of them, his true and lawful attorneys-in-fact, each with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities and Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

| <b>Signature</b>   | <b>Title</b>  | <b>Date</b>    |
|--|---|----------------|
| /s/ Robert I. Blum<br>Robert I. Blum                     | President, Chief Executive Officer and<br>Director (Principal Executive Officer)                                | March 12, 2008 |
| /s/ Sharon Surrey-Barbari<br>Sharon Surrey-Barbari       | Senior Vice President, Finance and Chief<br>Financial Officer (Principal Financial and<br>Accounting Executive) | March 12, 2008 |
| /s/ James Sabry, M.D., Ph.D.<br>James Sabry, M.D., Ph.D. | Executive Chairman and Director   | March 12, 2008 |
| /s/ Stephen Dow<br>Stephen Dow                           | Director  | March 12, 2008 |
| /s/ A. Grant Heidrich, III                               | Director  | March 12, 2008 |

A. Grant Heidrich, III

/s/ Charles Homcy, M.D.

Director

March 12, 2008

Charles Homcy, M.D.

/s/ Mark McDade

Director

March 12, 2008

Mark McDade

/s/ Michael Schmertzler

Director

March 12, 2008

Michael Schmertzler

/s/ James A. Spudich, Ph.D

Director

March 12, 2008

James A. Spudich, Ph.D

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| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| 3.1                       | Amended and Restated Certificate of Incorporation.(1)   |
| 3.2                       | Amended and Restated Bylaws.(1)   |
| 4.1                       | Specimen Common Stock Certificate.(20)  |
| 4.2                       | Fourth Amended and Restated Investors Rights Agreement, dated March 21, 2003, by and among the Company and certain stockholders of the Registrant.(1)   |
| 4.3                       | Master Security Agreement, dated February 2, 2001, by and between the Company and General Electric Capital Corporation.(1)  |
| 4.4                       | Cross-Collateral and Cross-Default Agreement by and between the Company and General Electric Capital Corporation.(1)  |
| 4.5                       | Warrant for the purchase of shares of common stock, dated July 20, 1999, issued by the Company to Bristow Investments, L.P.(1)  |
| 4.6                       | Warrant for the purchase of shares of common stock, dated July 20, 1999, issued by the Company to the Laurence and Magdalena Shushan Family Trust.(1)   |
| 4.7                       | Warrant for the purchase of shares of common stock, dated July 20, 1999, issued by the Company to Slough Estates USA Inc.(1)  |
| 4.9                       | Warrant for the purchase of shares of common stock, dated October 28, 2005, issued by the Company to Kingsbridge Capital Limited.(9)  |
| 4.10                      | Registration Rights Agreement, dated October 28, 2005, by and between the Company and Kingsbridge Capital Limited.(9)   |
| 4.11                      | Registration Rights Agreement, dated as of December 29, 2006, by and between the Company and Amgen Inc. (16)  |
| 4.12                      | Warrant for the purchase of shares of common stock, dated October 15, 2007, issued by the Company to Kingsbridge Capital Limited.(19)   |
| 4.13                      | Registration Rights Agreement, dated October 15, 2007, by and between the Company and Kingsbridge Capital Limited.(19)  |
| 10.1                      | Form of Indemnification Agreement between the Company and each of its directors and officers.(1)  |
| 10.2                      | 1997 Stock Option/Stock Issuance Plan.(1)   |
| 10.3                      | 2004 Equity Incentive Plan.(1)  |
| 10.4                      | 2004 Employee Stock Purchase Plan.(1)   |
| 10.5                      | Build-to-Suit Lease, dated May 27, 1997, by and between Britannia Pointe Grand Limited Partnership and Metaxen, LLC.(1)   |
| 10.6                      | First Amendment to Lease, dated April 13, 1998, by and between Britannia Pointe Grand Limited Partnership and Metaxen, LLC.(1)  |
| 10.7                      | Sublease Agreement, dated May 1, 1998, by and between the Company and Metaxen LLC.(1)   |
| 10.8                      | Sublease Agreement, dated March 1, 1999, by and between Metaxen, LLC and Exelixis Pharmaceuticals, Inc.(1)  |
| 10.9                      | Assignment and Assumption Agreement and Consent, dated July 11, 1999, by and among Exelixis Pharmaceuticals, Metaxen, LLC, Xenova Group PLC and Britannia Pointe Grande Limited Partnership.(1) |
| 10.10                     | Second Amendment to Lease, dated July 11, 1999, by and between Britannia Pointe Grand Limited Partnership and Exelixis Pharmaceuticals, Inc.(1)   |
| 10.11                     | First Amendment to Sublease Agreement, dated July 20, 1999, by and between the Company and Metaxen.(1)  |
| 10.12                     | Agreement and Consent, dated July 20, 1999, by and among Exelixis Pharmaceuticals, Inc., the Company and Britannia Pointe Grand Limited Partnership.(1)   |

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- 10.13 Amendment to Agreement and Consent, dated July 31, 2000, by and between the Company, Exelixis, Inc., and Britannia Pointe Grande Limited Partnership.(1)
  - 10.14 Assignment and Assumption of Lease, dated September 28, 2000, by and between Exelixis, Inc. and the Company.(1)
  - 10.15 Sublease Agreement, dated September 28, 2000, by and between the Company and Exelixis, Inc.(1)
-

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| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| 10.16                     | Sublease Agreement, dated December 29, 1999, by and between the Company and COR Therapeutics, Inc.(1)   |
| *10.17                    | Collaboration and License Agreement, dated June 20, 2001, by and between the Company and Glaxo Group Limited.(1)  |
| *10.18                    | Memorandum, dated June 20, 2001, by and between the Company and Glaxo Group Limited.(1)   |
| *10.19                    | Letter Amendment to Collaboration Agreement, dated October 28, 2002, by and between the Company and Glaxo Group Limited.(1)   |
| *10.20                    | Letter Amendment to Collaboration Agreement, dated November 5, 2002, by and between the Company and Glaxo Group Limited.(1)   |
| *10.21                    | Letter Amendment to Collaboration Agreement, dated December 13, 2002, by and between the Company and Glaxo Group Limited.(1)  |
| *10.22                    | Letter Amendment to Collaboration Agreement, dated July 11, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| *10.23                    | Letter Amendment to Collaboration Agreement, dated July 28, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| *10.24                    | Letter Amendment to Collaboration Agreement, dated July 28, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| *10.25                    | Letter Amendment to Collaboration Agreement, dated July 28, 2003, by and between the Company and Glaxo Group Limited.(1)  |
| 10.26                     | Series D Preferred Stock Purchase Agreement, dated June 20, 2001, by and between the Company and Glaxo Wellcome International B.V.(1)   |
| 10.27                     | Amendment No. 1 to Series D Preferred Stock Purchase Agreement, dated April 2, 2003, by and among the Company, Glaxo Wellcome International B.V. and Glaxo Group Limited.(1)              |
| *10.28                    | Exclusive License Agreement between The Board of Trustees of the Leland Stanford Junior University, The Regents of the University of California, and the Company dated April 21, 1998.(1) |
| 10.29                     | Modification Agreement between The Regents of the University of California, The Board of Trustees of the Leland Stanford Junior University and the Company, dated September 1, 2000.(1)   |
| *10.30                    | Collaboration and License Agreement, dated December 15, 2003, by and between AstraZeneca AB and the Company.(1)   |
| 10.31                     | David J. Morgans and Sandra Morgans Promissory Note, dated May 20, 2002.(1)   |
| 10.32                     | David J. Morgans and Sandra Morgans Promissory Note, dated October 18, 2000.(1)   |
| 10.33                     | James H. Sabry and Sandra J. Spence Promissory Note, dated November 12, 2001.(1)  |
| 10.34                     | Robert I. Blum Cash Bonus Agreement, dated September 1, 2002.(1)  |
| 10.35                     | Robert I. Blum Amended and Restated Cash Bonus Agreement, dated December 1, 2003.(1)  |
| 10.36                     | David J. Morgans Cash Bonus Agreement, dated September 1, 2002.(1)  |
| 10.37                     | David J. Morgans Amended and Restated Cash Bonus Agreement, dated December 1, 2003.(1)  |
| 10.38                     | Jay K. Trautman Cash Bonus Agreement, dated September 1, 2002.(1)   |
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| 10.40                     | Common Stock Purchase Agreement, dated March 10, 2004, by and between the Company and Glaxo Group Limited.(1)   |
| *10.41                    | Collaboration and Facilities Agreement, dated August 19, 2004, by and between the Company and Portola Pharmaceuticals, Inc.(2)  |
| 10.42                     | Executive Employment Agreement, dated July 8, 2004, by and between the Company and Jay Trautman.(2)   |
| 10.43                     |   |



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- Executive Employment Agreement, dated July 14, 2004, by and between the Company and James Sabry.(2)
- 10.44 Executive Employment Agreement, dated July 14, 2004, by and between the Company and David Morgans.(2)
- 10.45 Executive Employment Agreement, dated September 1, 2004, by and between the Company and Robert Blum.(2)
-

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| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| 10.46                     | Executive Employment Agreement, dated September 7, 2004, by and between the Company and Sharon Surrey-Barbari.(2)   |
| 10.47                     | Executive Employment Agreement, dated as of August 22, 2005, by and between the Company and Andrew Wolff.(7)  |
| 10.48                     | Executive Employment Agreement, dated February 1, 2005, by and between the Company and David Cragg.(10)   |
| *10.49                    | First Amendment to Collaboration and Facilities Agreement, dated March 24, 2005, by and between the Company and Portola Pharmaceuticals, Inc.(3)                          |
| *10.50                    | Amendment to the Collaboration and License Agreement with GlaxoSmithKline, effective as of September 21, 2005, by and between the Company and Glaxo Group Limited.(5)     |
| 10.51                     | Sublease, dated as of November 29, 2005, by and between the Company and Millennium Pharmaceuticals, Inc.(6)   |
| 10.52                     | Common Stock Purchase Agreement, dated as of October 28, 2005, by and between the Company and Kingsbridge Capital Limited.(9)   |
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| 24.1                      | Power of Attorney (see page 113)  |
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- (3) Incorporated by reference from our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on May 12, 2005.
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