

CYTOKINETICS INC
Form 10-K
March 12, 2009

Table of Contents

**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, 2008**
- 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:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, \$0.001 par value	The NASDAQ Global Market

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

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 filer <input checked="" type="radio"/>	Non-accelerated filer <input type="radio"/> (Do not check if a smaller reporting company)	Smaller reporting company <input type="radio"/>
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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 \$129.7 million computed by reference to the last sales price of \$3.71 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, 2008. 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 27, 2009 was 53,219,291 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2009 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.

CYTOKINETICS, INCORPORATED

**FORM 10-K
Year Ended December 31, 2008**

INDEX

	Page
<u>PART I</u>	
<u>Item 1.</u> <u>Business</u>	3
<u>Item 1A.</u> <u>Risk Factors</u>	21
<u>Item 1B.</u> <u>Unresolved Staff Comments</u>	42
<u>Item 2.</u> <u>Properties</u>	43
<u>Item 3.</u> <u>Legal Proceedings</u>	43
<u>Item 4.</u> <u>Submission of Matters to a Vote of Security Holders</u>	43
<u>PART II</u>	
<u>Item 5.</u> <u>Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	44
<u>Item 6.</u> <u>Selected Financial Data</u>	46
<u>Item 7.</u> <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	47
<u>Item 7A.</u> <u>Quantitative and Qualitative Disclosures About Market Risk</u>	67
<u>Item 8.</u> <u>Financial Statements and Supplementary Data</u>	70
<u>Item 9.</u> <u>Changes in and Disagreements With Accountants on Accounting and Financial Disclosure</u>	109
<u>Item 9A.</u> <u>Controls and Procedures</u>	109
<u>Item 9B.</u> <u>Other Information</u>	109
<u>PART III</u>	
<u>Item 10.</u> <u>Directors, Executive Officers and Corporate Governance</u>	110
<u>Item 11.</u> <u>Executive Compensation</u>	110
<u>Item 12.</u> <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	110
<u>Item 13.</u> <u>Certain Relationships and Related Transactions, and Director Independence</u>	110
<u>Item 14.</u> <u>Principal Accountant Fees and Services</u>	110
<u>PART IV</u>	
<u>Item 15.</u> <u>Exhibits and Financial Statement Schedules</u>	111
<u>Signatures</u>	116
<u>EX-10.55</u>	
<u>EX-10.62</u>	
<u>EX-10.63</u>	
<u>EX-10.64</u>	
<u>EX-10.65</u>	
<u>EX-10.66</u>	

EX-10.67
EX-10.68
EX-23.1
EX-31.1
EX-31.2
EX-32.1

Table of Contents

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:

guidance concerning revenues, research and development expenses and general and administrative expenses for 2009;

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

our capital requirements and needs for additional financing;

the results from the clinical trials that we have conducted with CK-1827452, and whether such results may result in Amgen Inc. (Amgen) exercising its option with respect to CK-1827452;

the initiation, progress, timing and scope of clinical trials and development activities for our drug candidates and potential drug candidates by ourselves or our partners, including the anticipated timing for initiation of clinical trials and anticipated dates of data becoming available or being announced from clinical trials;

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

our and our partners' plans or ability for the continued research and development of our drug candidates and potential drug candidates, such as CK-1827452, ispinesib, SB-743921, GSK-923295 and CK-2017357;

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

the properties and potential benefits of, and the potential market opportunities for, our drug candidates and potential drug candidates;

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

the sufficiency of the clinical trials conducted with our drug candidates to demonstrate that they are safe and efficacious;

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

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

the issuance of shares of our common stock under our committed equity financing facility entered into with Kingsbridge Capital Limited (Kingsbridge) in 2007;

our ability to protect our intellectual property and to avoid infringing the intellectual property rights of others;
expected future sources of revenue and capital;
losses, costs, expenses and expenditures;
future payments under lease obligations and equipment financing lines;
potential competitors and competitive products;
increasing the number of our employees and recruiting additional key personnel;
expected future amortization of employee stock-based compensation; and
our ability to sell equipment held for sale and the timing of such sales.

Table of Contents

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

our ability to obtain additional financing;

difficulties or delays in the development, testing, production or commercialization of our drug candidates, including decisions by GSK to postpone or discontinue research or development activities relating to 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 preclinical studies or clinical trials may not be indicative of future clinical trials results);

the possibility that the U.S. Food and Drug Administration (FDA) or foreign regulatory agencies may delay or limit our or our partners' ability to conduct clinical trials or may delay or withhold approvals for the manufacture and sale of our products;

our receipt of funds under our strategic alliances, including those funds dependent upon Amgen's potential exercise of its option with respect to CK-1827452;

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

our ability to maintain the effectiveness of our registration statement permitting resale of securities to be issued to Kingsbridge by us under, and in connection with, our 2007 committed equity financing facility;

changing standards of care and the introduction of products by competitors or alternative therapies for the treatment of indications we target that may make our drug candidates commercially unviable;

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

potential infringement by us 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 reported 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, are registered service marks and trademarks 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 were incorporated in Delaware in August 1997 as Cytokinetics, Incorporated. We are a clinical-stage biopharmaceutical company focused on the discovery and development of novel small molecule therapeutics that modulate muscle function for the potential treatment of serious diseases and medical conditions. Our research and development activities relating to the biology of muscle function have evolved from our knowledge and expertise regarding the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. Our current research and development programs relating to the biology of muscle function are directed to small molecule modulators of the contractility of cardiac, skeletal and smooth muscle. Our cardiac muscle contractility program is focused on cardiac muscle myosin, a motor protein that powers cardiac muscle contraction. Our lead drug candidate from this program, CK-1827452, is a novel cardiac muscle myosin activator. CK-1827452 entered Phase IIa clinical trials for the treatment of heart failure in 2007. We have granted Amgen an option for an exclusive license to develop and commercialize CK-1827452 world-wide, except Japan, subject to our development and

Table of Contents

commercialization participation rights. Further details regarding our strategic alliance with Amgen can be found below in Item 1 of this report under **Muscle Contractility Focus Cardiac Muscle Contractility Program Amgen Collaboration and Option Agreement**.

In April 2008, we announced the selection of a potential drug candidate, CK-2017357, an activator of the skeletal muscle sarcomere, the basic unit of skeletal muscle contraction. We believe CK-2017357 may be useful in treating diseases or medical conditions associated with skeletal muscle weakness or wasting. We have also designated a second, structurally distinct skeletal muscle sarcomere activator for development as a backup compound to CK-2017357. Both of these compounds activate the skeletal muscle troponin complex, which is a set of regulatory proteins that modulates the contractility of the skeletal sarcomere.

In January 2009, we announced the selection of a potential drug candidate that modulates smooth muscle contractility. This compound is a direct inhibitor of smooth muscle myosin, the motor protein central to the contraction of smooth muscle, that causes the relaxation of contracted smooth muscle. Specifically intended for inhaled delivery applications, this compound may be developed as a potential treatment for pulmonary arterial hypertension and diseases associated with bronchoconstriction.

Our initial research activities were directed to mitotic kinesins, a family of cytoskeletal motor proteins involved in the process of cell division, or mitosis. This research produced three drug candidates currently in clinical testing for the potential treatment of cancer: ispinesib, SB-743921 and GSK-923295. Ispinesib and SB-743921 are structurally distinct inhibitors of kinesin spindle protein and GSK-923295 is an inhibitor of centromere-associated protein E. We are currently conducting the Phase I portion of a Phase I/II clinical trial of ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer and the Phase I portion of a Phase I/II trial of SB-743921 in patients with non-Hodgkin or Hodgkin lymphoma. Under a strategic alliance established in 2001, GSK is conducting a Phase I clinical trial with GSK-923295. Further details regarding our strategic alliance with GSK can be found below in Item 1 of this report under **Oncology Program: Mitotic Kinesin Inhibitors GSK Strategic Alliance**.

Following is a summary of the status of our drug candidates and potential drug candidates. All development is being conducted by Cytokinetics, except where otherwise noted:

Muscle Contractility Programs

Compound	Mode of Administration	Development Stage	Potential Indication(s)	Planned 2009 Activities
CK-1827452 * (cardiac muscle myosin activator)	oral, intravenous	Phase II	heart failure	initiate a Phase IIa pharmacokinetic clinical trial of a modified release and an immediate release formulation in Q2 2009 initiate 1st Phase IIb clinical trial in mid-2009 continue Phase IIa clinical trial in heart failure patients undergoing cardiac catheterization

CK-2017357 (skeletal sarcomere activator)	oral	IND-enabling studies	Diseases and conditions associated with muscle weakness or wasting, e.g., amyotrophic lateral sclerosis, sarcopenia, cachexia	submit IND initiate Phase I clinical trial in healthy volunteers
smooth muscle myosin inhibitor	inhaled	IND-enabling studies	pulmonary arterial hypertension, asthma, chronic obstructive pulmonary disease	continue IND-enabling studies

* CK-1827452 is being developed by Cytokinetics, subject to Amgen's option to develop and commercialize world-wide, except Japan.

Table of Contents***Oncology Programs***

Compound	Mode of Administration	Development Stage	Potential Indication(s)	Planned 2009 Activities
ispinesib (kinesin spindle protein inhibitor)	intravenous	Phase I	breast cancer	continue Phase I of a Phase I/II clinical trial
SB-743921 (kinesin spindle protein inhibitor)	intravenous	Phase I	Hodgkin and non-Hodgkin lymphomas	continue Phase I of a Phase I/II clinical trial
GSK-923295 ** (centromere-associated protein E inhibitor)	intravenous	Phase I	cancer	GSK to continue Phase I clinical trial in patients with advanced, refractory solid tumors GSK anticipated to initiate a Phase II clinical trial

** GSK-923295 is being developed by GSK under our strategic alliance.

All of our drug candidates and potential drug candidates have grown out of our cytoskeletal research activities. Our focus on the biology of the cytoskeleton distinguishes us from other biopharmaceutical companies, and potentially positions us to discover and develop novel therapeutics that may be useful for the treatment of severe diseases and medical conditions. We believe that this focus and the resulting knowledge and expertise that we have developed, especially with our proprietary technologies that permit us to evaluate the function of cytoskeletal proteins in high information content biological assays, has allowed us to increase the efficiency of our drug discovery activities. Our research and development activities since our inception in 1997 have produced four drug candidates currently in clinical testing and three potential drug candidates currently in preclinical development. Each of has a novel mechanism of action compared to currently marketed drugs, which we believe validates our focus on the cytoskeleton as a robust area for drug discovery. We intend to leverage our experience in muscle contractility in order to expand our current pipeline, and expect to continue to be able to identify additional potential drug candidates that may be suitable for clinical development.

Our Corporate Strategy

Our strategy is to discover, develop and commercialize novel drug products that modulate muscle function in ways that may benefit patients with disorders that cause serious diseases or medical conditions, with the goal of establishing a fully integrated biopharmaceutical company. We intend to achieve this by:

Focusing on drug discovery and development activities relating to the biology of muscle function. We intend to capitalize on the knowledge and expertise we acquired in each of our cardiac, smooth and skeletal muscle research and development programs. In these programs, we are investigating potential treatments for diseases

or medical conditions where dysregulation of the contractile function of muscle plays a key role and may be amenable to treatment by modulation of muscle contractility, such as heart failure and medical conditions associated with skeletal muscle weakness or wasting.

Leveraging our cytoskeletal expertise and proprietary technologies to increase the speed, efficiency and yield of our drug discovery and development processes. We believe that our unique understanding of the cytoskeleton and our proprietary research technologies should enable us to discover and potentially to develop drug candidates with novel mechanisms of action that may offer potential benefits not provided by existing drugs. We expect that we may be able to leverage our expertise in muscle contractility to develop programs that relate to other muscle functions and similarly may impact serious medical diseases and conditions. This may facilitate our building a diversified pipeline of drug candidates in a cost-effective way while managing risk.

Building development and commercialization capabilities directed at concentrated markets. We focus our drug discovery and development activities on disease areas where there are serious unmet medical needs. In particular, we direct our activities to potential commercial opportunities in concentrated and tractable customer segments, such as hospital specialists, that may be addressed by a smaller, targeted sales force. In

Table of Contents

this manner, we believe that a company with limited resources may be able to compete effectively against larger, more established companies with greater financial and commercial resources. For these opportunities, we intend to develop clinical development and sales and marketing capabilities with the goal of becoming a fully-integrated biopharmaceutical company.

Establishing select strategic alliances to support our drug development programs while preserving significant development and commercialization rights. We believe that such alliances may allow us to obtain financial support and to capitalize on the therapeutic area expertise and resources of our partners that can potentially accelerate the development and commercialization of our drug candidates. Where we deem appropriate, we plan to retain certain rights to participate in the development of drug candidates and commercialization of potential drugs arising from our alliances, so that we can expand and capitalize on our internal development capabilities and build our commercialization capabilities.

Muscle Contractility Focus

Our long-standing interest in the cytoskeleton has led us to focus our research and development activities on the biology of muscle function, and in particular, small molecule modulation of muscle contractility. We believe that our expertise in the modulation of the contractility of each of cardiac, skeletal and smooth muscle is an important differentiator for us. Our established preclinical and clinical expertise in muscle contractility may position us to discover and develop additional novel therapies that have the potential to improve the health of patients with severe and debilitating diseases or medical conditions.

Small molecules that affect muscle contractility may have several applications for a variety of serious diseases and medical conditions. For example, heart failure is a disease often characterized by impaired cardiac muscle contractility which may be treated by modulating the contractility of cardiac muscle; certain neuromuscular diseases and medical conditions associated with muscle weakness may be amenable to treatment by enhancing the contractility of skeletal muscle; hypertension is a disease in which elevated blood pressure may be decreased by relaxation of the arterial smooth muscle; and asthma is a disease in which constriction of the airways may be treated by relaxation of the airway smooth muscle.

Because each muscle type may be relevant to multiple diseases or medical conditions, we believe we can leverage our expertise in each of cardiac, skeletal and smooth muscle contractility to more efficiently discover and develop as potential drugs compounds that modulate the applicable muscle type for multiple indications. In addition, muscle has biological functions other than contractility. Accordingly, our knowledge and expertise could also serve as an entry point to the discovery of novel treatments for disorders involving muscle functions other than muscle contractility, such as muscle metabolism and energetics.

We are currently developing four small molecule compounds arising from our muscle contractility programs. CK-1827452, a novel cardiac muscle myosin activator, is currently in Phase IIa clinical trials for the potential treatment of heart failure. CK-2017357 is our lead potential drug candidate from our skeletal muscle contractility program. We are evaluating the potential indications for which this compound may be useful. These may include skeletal muscle weakness associated with neuromuscular diseases and other medical conditions characterized by skeletal muscle weakness or wasting. We plan to submit an investigational new drug application (IND) with the FDA to initiate a Phase I clinical trial for CK-2017357 in 2009. We have selected a second potential drug candidate from this program that may serve as a backup compound to CK-2017357. We are also developing an inhaled inhibitor of smooth muscle myosin as a bronchodilator, which is currently in IND-enabling studies. We are continuing to conduct discovery, characterization and lead optimization activities for other compounds with the potential to modulate muscle contractility and other muscle functions.

Cardiac Muscle Contractility Program

Overview. Our cardiac muscle contractility program is focused on the cardiac sarcomere, the basic unit of muscle contraction in the heart. The cardiac sarcomere is a highly ordered cytoskeletal structure composed of cardiac muscle myosin, actin and a set of regulatory proteins. This program is currently directed towards the discovery and development of small molecule cardiac muscle myosin activators with the goal of developing novel drugs to treat acute and chronic heart failure. Cardiac muscle myosin is the cytoskeletal motor protein in the cardiac

Table of Contents

muscle cell. It is directly responsible for converting chemical energy into the mechanical force, resulting in cardiac muscle contraction. This program is based on the hypothesis that activators of cardiac muscle myosin may address certain adverse properties of existing positive inotropic agents. Current positive inotropic agents, such as beta-adrenergic receptor agonists or inhibitors of phosphodiesterase activity, increase the concentration of intracellular calcium, thereby increasing cardiac sarcomere contractility. However, the increase in calcium levels increases the velocity of cardiac muscle contraction and shortens systolic ejection time, which has been linked to potentially life-threatening side effects. In contrast, our novel cardiac muscle myosin activators work by a mechanism that directly stimulates the activity of the cardiac muscle myosin motor protein, without increasing the intracellular calcium concentration. They accelerate the rate-limiting step of the myosin enzymatic cycle and shift it in favor of the force-producing state. Rather than increasing the velocity of cardiac contraction, this mechanism instead lengthens the systolic ejection time, which results in increased cardiac muscle contractility and cardiac output in a potentially more oxygen-efficient manner.

Background on Heart Failure Market. 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. It is estimated that in 2006, 5.5 million patients in the United States suffered from chronic heart failure. Approximately 4.5 million patients in the United States had a hospital discharge diagnosis of heart failure in 2007, of which over 2.4 million had a primary or secondary diagnosis of heart failure. These numbers are increasing due to the aging of the U.S. population and an increased likelihood of survival following acute myocardial infarctions. The costs to society attributable to the prevalence of heart failure are high, especially as many chronic heart failure patients suffer repeated acute episodes. Despite currently available therapies, readmission rates for heart failure patients over the age of 65 are as high as 42% within one year of hospital discharge. Mortality rates over the five-year period following a diagnosis of heart failure are approximately 60%. The limited effectiveness of current therapies points to the need for therapeutics that offer improved efficacy without increased adverse events, thus decreasing morbidity and mortality rates among this patient population. The annual cost of heart failure to the U.S. health care system is estimated to be \$35 billion dollars. A portion of that cost is attributable to drugs used to treat each of chronic and acute heart failure. Sales of drugs to treat chronic heart failure reached almost \$2.5 billion in 2006 while sales of drugs to treat acute heart failure reached over \$350 million in 2007.

CK-1827452. Our lead drug candidate from this program is CK-1827452, a novel cardiac muscle myosin activator. CK-1827452 has been the subject of a clinical trials program, initiated in 2007, comprised of Phase I and Phase IIa clinical trials 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 as an intravenous formulation for use in the hospital setting and as an oral formulation for use in the outpatient setting.

In 2006, we reported that in the first-time-in-humans Phase I clinical trial of CK-1827452 administered intravenously in healthy volunteers, CK-1827452 demonstrated statistically significant and concentration-dependent increases in indices of left ventricular function over a range of well-tolerated doses and plasma concentrations. In addition, CK-1827452 exhibited generally linear, dose-proportional pharmacokinetics across the dose range studied. The adverse effects observed at intolerable doses in humans appeared similar to the adverse findings which occurred in preclinical safety studies at similar plasma concentrations. These effects are believed to be related to the mechanism of action of this drug candidate which, at intolerable doses, resulted in an excessive prolongation of the systolic ejection time. However, these effects resolved promptly with discontinuation of the infusions of CK-1827452.

A Phase I oral bioavailability study of CK-1827452 in healthy volunteers conducted in 2006 demonstrated an oral bioavailability of approximately 100%, with no first-pass metabolism by the liver observed. Because the oral formulation of CK-1827452 used in this study was found to be rapidly absorbed, we are pursuing the development of

modified release oral formulations of CK-1827452 to achieve a reduced rate of drug absorption without significantly affecting the overall bioavailability.

Table of Contents

The following clinical trials of CK-1827452 were conducted or completed during 2008:

CK-1827452 (intravenous)

Phase IIa stable heart failure (safety and tolerability): Throughout 2008, we continued to conduct our ongoing Phase IIa clinical trial of CK-1827452 administered intravenously to patients with stable heart failure. The trial's primary objective is to evaluate 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. This clinical trial was planned to consist of five cohorts of eight patients with stable heart failure. We have completed treatment of Cohort 5 of this trial. In the first four cohorts, patients underwent four treatment periods, receiving three escalating active doses of CK-1827452, with one placebo treatment randomized into the dose escalation sequence to maintain blinding. In Cohort 5, patients had two treatment periods, receiving an active dose of CK-1827452 in one treatment period and a placebo treatment in the other.

We presented interim data from this trial at several scientific meetings in 2008, most recently at the Scientific Sessions of the American Heart Association in November 2008. The presentation included data from 28 patients (eight patients from each of Cohorts 1, 2 and 3 and four patients from Cohort 4), and showed statistically significant effects in measures of cardiac function. Specifically, these interim analyses demonstrated statistically significant increases in systolic ejection time and fractional shortening at CK-1827452 plasma concentrations greater than 100 ng/mL, and statistically significant increases in stroke volume at CK-1827452 plasma concentrations greater than 200 ng/mL. There were also statistically significant increases in ejection fraction at CK-1827452 plasma concentrations greater than 300 ng/mL when ejection fraction was calculated by a hybrid method in which stroke volume, measured using Doppler technology, was divided by the left ventricular end-diastolic volume, measured using two-dimensional echocardiography. In addition, the data demonstrated statistically significant correlations between increasing CK-1827452 plasma concentration and increases in systolic ejection time, stroke volume, fractional shortening, ejection fraction and cardiac output and between increasing CK-1827452 plasma concentration and decreases in supine and standing heart rate and left ventricular end-systolic volume. In this trial, CK-1827452 was well-tolerated in stable heart failure patients over a range of plasma concentrations during continuous intravenous administration. These data reflect what we believe is the clinically relevant activity of this novel drug candidate. We anticipate presenting final data from this clinical trial at the Annual Meeting of the American College of Cardiology in March 2009.

Phase IIa stable heart failure (cardiac catheterization): Preclinical studies have suggested that CK-1827452 increases ventricular performance in the absence of substantial changes in cardiac muscle oxygen consumption, thereby increasing cardiac muscle efficiency. In 2008, we initiated an open-label, non-randomized Phase IIa clinical trial designed to evaluate CK-1827452 administered intravenously to patients with stable heart failure undergoing clinically indicated coronary angiography in order to corroborate this preclinical finding in humans. In September 2008, a poster outlining the design of this clinical trial was presented at the annual Heart Failure Society of America Conference. The first cohort, consisting of six patients, is planned to undergo a dose-escalation phase, beginning with a target plasma concentration of approximately 280 ng/mL. Based on the tolerability and pharmacodynamic effects observed in this initial cohort, the investigators will select a single dosing regimen for the second and final cohort of twelve patients. We are continuing to enroll patients in the first cohort of this trial.

CK-1827452 (oral):

Phase I drug-drug interaction: In June 2008 and December 2008, we announced results from a Phase I clinical trial in healthy male subjects evaluating the potential for certain drug-drug interactions mediated by the drug-metabolizing enzymes cytochrome P450 3A4 and cytochrome P450 2D6. Results showed that there were no clinically important differences observed between subjects who were extensive or poor metabolizers with respect to their defined genotype

for cytochrome P450 2D6. No clinically meaningful pharmacokinetic drug-drug interactions with either ketoconazole, a potent inhibitor of cytochrome P450 3A4, or diltiazem, a moderate inhibitor of cytochrome P450 3A4, were identified in either extensive metabolizer or poor metabolizer subjects with respect to cytochrome P450 2D6.

Table of Contents

Phase I oral single to multi-dose: In June 2008, we announced final results from a Phase I clinical trial evaluating CK-1827452 administered as a single oral dose and as multiple oral doses of 10 mg and 30 mg strength capsules. The primary objective of this study was to evaluate the safety and tolerability of CK-1827452 after a single oral dose and after multiple oral doses to steady-state in healthy men and women. The secondary objectives of this study were to evaluate the pharmacokinetics of CK-1827452 after a single oral dose and after multiple oral doses to steady-state and to compare the pharmacokinetic parameters between healthy men and women. CK-1827452 was well-tolerated in the trial, with no drug-related serious adverse events. Dose-proportionality between the 10 mg and 30 mg dose levels was observed in both men and women, both after a single dose and after multiple doses to steady-state, with similar pharmacokinetics observed in men and women.

Phase I modified release: In June 2008, we announced results from a Phase I clinical trial evaluating the pharmacokinetics and relative bioavailability of three different oral modified release prototype formulations of CK 1827452, as compared to the immediate release formulation, in healthy male subjects. The single-dose pharmacokinetics of each of these formulations, in both the fasted and fed states, demonstrated that, as compared to the immediate release formulation, they reduced the maximum CK-1827452 plasma concentration and elevated the trough plasma concentration without a substantial effect on overall bioavailability. This resulted in a smaller range of fluctuation in plasma concentrations as compared to oral dosing with the immediate release formulation. We have selected one prototype modified release formulation to proceed forward into further clinical testing.

CK-1827452 (intravenous-to-oral):

Phase IIa ischemic cardiomyopathy and angina (safety and tolerability): In April 2008 we initiated, and in December 2008 we announced, results from a double-blind, randomized, placebo-controlled Phase IIa clinical trial designed to evaluate an intravenous and an oral formulation of CK-1827452 in patients with ischemic cardiomyopathy and angina. The primary objective of this trial was to assess the effect of intravenous CK-1827452 on symptom-limited treadmill exercise tolerance. The secondary objective of this trial was to assess the tolerability and resulting plasma concentrations of CK-1827452 administered as an oral formulation. The trial was designed to evaluate two cohorts of 45 patients, each with ischemic cardiomyopathy and angina and an ejection fraction of less than or equal to 35 percent. In each cohort, patients whose symptom-limited exercise tolerance during an infusion of double-blind study drug did not deteriorate relative to a baseline treadmill exercise test received either CK-1827452 or placebo administered orally for seven days. CK-1827452 plasma levels were measured during the infusions and before and one hour after the final oral dose. Patients in the first cohort were randomized in a 2-to-1 ratio to CK-1827452 versus placebo, at a dose level intended to target a maximum plasma concentration of 295 ng/ml during the infusion and 184 ng/ml during oral dosing. Patients in the second cohort were randomized in a 2-to-1 ratio to CK-1827452 versus placebo, at a dose level intended to target a plasma concentration of 550 ng/ml during the infusion and 368 ng/ml during oral dosing.

A total of 94 patients were enrolled and treated in this clinical trial; 29 patients received placebo, 31 received CK-1827452 at the lower dose level, and 34 received CK-1827452 at the higher dose level. The primary safety endpoint was defined as stopping an exercise treadmill test during double-blind treatment with CK-1827452 or placebo due to unacceptable angina at an exercise stage earlier than at baseline. This endpoint was observed in one patient receiving placebo and did not occur in any patient receiving CK-1827452 at either dose level. Twenty-one of 27 unique adverse events observed in this trial were reported as mild in severity, 4 were reported as moderate and 2 were reported as severe. Of the 94 patients treated, 19 reported at least one unique adverse event at any time during the trial: 5 patients on placebo; 2 patients on the lower dose level of CK-1827452; and 12 patients on the higher dose level of CK-1827452, who reported a total of 18 unique adverse events (15 of which were reported as mild in severity). The 2 severe adverse events were the only serious adverse events reported. Both occurred in the same patient, who received intravenous CK-1827452 in Cohort 2. Both these events were judged by the investigator to have been unrelated to treatment with CK-1827452. We anticipate that final data from this clinical trial will be presented in

2009.

Planned Clinical Development. We believe the safety data from our Phase IIa clinical trial evaluating the safety and tolerability of CK-1827452 in patients with ischemic cardiomyopathy and angina, together with the improvements in systolic function observed in our Phase IIa clinical trial evaluating the safety and tolerability of CK-1827452 in stable heart failure patients, support the progression of CK-1827452 into Phase IIb clinical

Table of Contents

development. In mid-2009, we anticipate the initiation of a Phase IIb clinical trial of CK-1827452 in chronic heart failure outpatients at increased risk for death and hospitalization. In the second quarter of 2009, we anticipate initiating an additional Phase IIa clinical trial designed to evaluate the pharmacokinetics of both a modified release and an immediate release formulation of CK-1827452 in patients with heart failure.

Amgen Collaboration and Option Agreement. 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. The agreement also granted Amgen an option to obtain an exclusive license world-wide, except Japan, to develop and commercialize CK-1827452 and other drug candidates arising from the collaboration. Amgen's option is exercisable during a defined period, the ending of which is dependent upon the satisfaction of certain conditions, primarily our delivery of certain Phase I and Phase IIa clinical data for CK-1827452 in accordance with an agreed development plan, the results of which may reasonably support its progression into Phase IIb clinical development. In February 2009, we announced that we believe we completed delivery of this data to Amgen. Prior to the exercise or expiration of Amgen's option, we are responsible for conducting all development activities for CK-1827452, at our own expense.

To exercise its option, Amgen would pay an exercise fee of \$50.0 million and thereafter would be responsible for the development and commercialization of CK-1827452 and related compounds, at its expense, subject to Cytokinetics development and commercialization participation rights. Following exercise of the option, the agreement provides for potential 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, and 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 entitled to co-promote CK-1827452 in North America and participate in agreed commercialization activities in institutional care settings, at Amgen's expense. If Amgen elects not to exercise its option to CK-1827452, we may then independently proceed to develop and commercialize CK-1827452, ourselves or with one or more other partners.

Skeletal Muscle Contractility Program

Overview. Our skeletal muscle contractility program is focused on the activation of the skeletal sarcomere, the basic unit of skeletal muscle contraction. The skeletal sarcomere is a highly ordered cytoskeletal structure composed of skeletal muscle myosin, actin, and a set of regulatory proteins, which include the troponins and tropomyosin. This program leverages our expertise developed in our ongoing discovery and development of cardiac sarcomere activators, including the cardiac muscle myosin activator CK-1827452.

Our skeletal sarcomere activators have demonstrated pharmacological activity that may lead to new therapeutic options for diseases and medical conditions associated with aging, muscle weakness and wasting and neuromuscular dysfunction. The clinical effects of muscle weakness and wasting, fatigue and loss of mobility can range from decreased quality of life to, in some instances, life-threatening complications. By directly improving skeletal muscle function, a small molecule activator of the skeletal sarcomere potentially could enhance functional performance and quality of life in patients suffering from diseases or medical conditions characterized or complicated by muscle weakness or wasting. These could include, but are not limited to, neuromuscular diseases such as amyotrophic lateral sclerosis, also known as ALS or Lou Gehrig's disease, cachexia in connection with heart failure or cancer, claudication, sarcopenia and general frailty associated with aging.

Potential drug candidates. In April 2008, we announced that we had selected CK-2017357 as the lead potential drug candidate from this program. We expect to submit an IND with the FDA to initiate a Phase I clinical trial of

CK-2017357 in healthy volunteers in 2009. In January 2009, we announced that we had selected another compound from this program as a backup development compound to CK-2017357. CK-2017357 and its backup development compound are structurally distinct small molecule activators of the skeletal sarcomere. These potential drug candidates act on the troponin regulatory complex of the skeletal sarcomere. Activation of the

Table of Contents

troponin complex increases its sensitivity to calcium, leading to an increase in skeletal muscle contractility. This mechanism of action has demonstrated encouraging pharmacological activity in preclinical models.

Ongoing research in skeletal muscle activators. Our research on the direct activation of skeletal muscle continues in two areas. We are conducting translational research with our existing series of skeletal sarcomere activators to explore the potential applications of this novel approach in preclinical studies. In addition, we have a research program aimed at the discovery and validation of other chemically and pharmacologically distinct mechanisms to activate the skeletal sarcomere.

Smooth Muscle Contractility Program

Overview. Smooth muscle is a non-striated form of muscle that is found in the circulatory, respiratory, digestive and genitourinary organ systems and is responsible for the contractile properties of these tissues. Because the contractile elements in non-striated muscle are not arranged into sarcomeres, the regulation of smooth muscle is different from that in cardiac and skeletal muscles. Smooth muscle contractility is driven by smooth muscle myosin, a cytoskeletal motor protein that is directly responsible for converting chemical energy into mechanical force. Our smooth muscle contractility program is focused on the discovery and development of small molecule smooth muscle myosin inhibitors, and leverages our expertise in muscle function and its application to drug discovery. Our inhaled smooth muscle myosin inhibitors have demonstrated pharmacological activity in preclinical models of bronchoconstriction and pulmonary vascular constriction and may have application for indications such as pulmonary arterial hypertension, asthma or chronic obstructive pulmonary disease. Our smooth muscle myosin inhibitors, administered orally or intravenously, have demonstrated pharmacological activity in preclinical models of systemic vascular constriction. Smooth muscle myosin inhibitors administered orally may have application in systemic hypertension

Potential drug candidate. In January 2009, we announced that we had selected a lead potential drug candidate from this program for advancement. This compound is a small molecule direct inhibitor of smooth muscle myosin. By inhibiting the function of the myosin motor protein central to smooth muscle contraction, this compound directly leads to the relaxation of contracted smooth muscle. Specifically intended for inhaled delivery applications, this potential drug candidate has demonstrated encouraging pharmacological activity in preclinical models as a novel mechanism vasodilator and bronchodilator. This data suggests that it may be useful as a potential treatment of diseases such as pulmonary arterial hypertension, asthma or chronic obstructive pulmonary disease. This potential drug candidate is currently in IND-enabling studies.

Ongoing research in smooth muscle myosin inhibitors. We are continuing to conduct early research activities to develop direct smooth muscle myosin inhibitor compounds for systemic administration for potential use in acute or chronic settings. Our research focus is to differentiate our compounds from existing drugs that are vasodilators that act by indirectly causing smooth muscle relaxation, such as commonly used calcium channel blockers. We are particularly interested in potential applications for our compounds where the benefits of currently available treatments are constrained by adverse side effects or limited effectiveness. For example, we are exploring the possible benefits of our smooth muscle inhibitors with respect to end-organ damage in the context of the potential treatment of systemic hypertension.

Oncology Program: Mitotic Kinesin Inhibitors

We currently have three drug candidates in clinical trials for the potential treatment of cancer: ispinesib, SB-743921 and GSK-923295. All of these arose from our earlier research activities directed to the role of the cytoskeleton in cell division and were progressed under our strategic alliance with GSK. This strategic alliance was established in 2001 to discover, develop and commercialize novel small molecule therapeutics targeting mitotic kinesins for applications in the treatment of cancer and other diseases. Mitotic kinesins are a family of cytoskeletal motor proteins involved in the

process of cell division, or mitosis. Under this strategic alliance, we focused primarily on two mitotic kinesins: kinesin spindle protein (KSP) and centromere-associated protein E (CENP-E).

We are currently conducting a Phase I/II clinical trial for each of ispinesib and SB-743921. Each of these is a structurally distinct small molecule that specifically inhibits KSP, interrupting cancer cell division and causing cell

Table of Contents

death. GSK's option to acquire a license to ispinesib and SB-743921 expired at the end of 2008. As a result, we have retained all rights to develop and commercialize ispinesib and SB-743921, subject to certain royalty obligations to GSK. We intend to complete the Phase I portion of our clinical trials for each of ispinesib and SB-743921. We are seeking a strategic partner for the future development and commercialization of these drug candidates.

GSK-923295 specifically inhibits CENP-E, interrupting cancer cell division and causing cell death. GSK is currently conducting a Phase I clinical trial of GSK-923295 in connection with our strategic alliance. We are conducting translational research directed to CENP-E jointly with GSK.

Background on Anti-Cancer Market. 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, and docetaxel from Sanofi-Aventis Pharmaceuticals Inc. Sales in the United States of taxanes alone were estimated to be \$2.8 billion in 2006.

Mitotic Kinesin Inhibitors. Since their introduction over 40 years ago, anti-mitotic drugs such as taxanes and vinca alkaloids have advanced the treatment of cancer and are commonly used for the treatment of several tumor types. However, these drugs have demonstrated limited treatment benefit against certain cancers. In addition, these drugs target tubulin, a cytoskeletal protein involved not only in mitosis and cell proliferation, but also in other important cellular functions. Inhibition of these other cellular functions produces dose-limiting toxicities such as peripheral neuropathy, an impairment of peripheral nervous system function.

Mitotic kinesins are also essential to mitosis, and, unlike tubulin, are not believed to be present in non-dividing cells. We believe that drugs that inhibit KSP, CENP-E and other mitotic kinesins may represent the next generation of anti-mitotic cancer drugs by arresting mitosis and cell proliferation without impacting unrelated, normal cellular functions, thereby avoiding many of the toxicities commonly experienced by patients treated with existing anti-mitotic drugs. 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 of ispinesib, SB-743921 and GSK-923295 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 observed was neutropenia, a decrease in the number of a certain type of white blood cell, which was generally reversible. Limited or no evidence of drug-related toxicities to the nervous system, heart, lung, kidney or liver was observed. We believe that this safety profile could potentially increase the therapeutic value of our mitotic kinesin inhibitors relative to other anti-mitotic drugs, and that a mitotic kinesin inhibitor drug candidate that is shown to have efficacy in one tumor type may also potentially have applications in other tumor types.

GSK Strategic Alliance. In 2001, we entered into a collaboration and license agreement with GSK which established a strategic alliance 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 the strategic alliance, GSK, in collaboration with the National Cancer Institute (NCI), conducted a broad Phase II clinical trials program designed to evaluate ispinesib across multiple tumor types. GSK also conducted a Phase I clinical trial of SB-743921. In November 2006, we amended the 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. GSK retained an option to resume responsibility for the development and commercialization of either or both of ispinesib and SB-743921. This option expired at the end of 2008. Accordingly, we retain all rights to both ispinesib and SB-743921, subject to certain royalty obligations to GSK.

GSK is currently conducting a Phase I clinical trial of 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, the royalties to be paid to us on future sales of GSK-923295 could potentially increase based on increasing product sales and our anticipated level of co-funding. If we

Table of Contents

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 commercialization activities.

In each of June 2006, 2007 and 2008, we amended the agreement to extend the research term of the GSK strategic alliance for an additional year to continue joint translational research directed to CENP-E.

Development Programs

Ispinesib

GSK and the NCI sponsored the initial clinical trials program for ispinesib, which consisted of nine Phase II clinical trials and eight Phase I or Ib clinical trials evaluating ispinesib in a variety of both solid and hematologic cancers. To date, we believe clinical activity for ispinesib has been observed in non-small cell lung, ovarian and breast cancers, with the most 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. In addition, preclinical and Phase Ib clinical data on ispinesib indicate that it may have an additive effect when combined with certain existing chemotherapeutic agents. As a result of the expiration of GSK's option relating to ispinesib, we have retained all development and commercialization rights to ispinesib. We are conducting a Phase I/II clinical trial for ispinesib to further define its clinical activity profile in chemotherapy-naïve locally advanced or metastatic breast cancer patients on a more dose-dense schedule than was previously evaluated to determine if the overall response to ispinesib can be increased while maintaining its existing safety profile. We intend to complete the Phase I portion of this trial. We are seeking a strategic partner for the future development and commercialization of ispinesib.

The following clinical trials for ispinesib were conducted or completed in 2008:

Breast Cancer: In December 2007, we initiated an open-label, non-randomized Phase I/II clinical trial designed to evaluate ispinesib as monotherapy administered 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 that had failed to respond or progressed after treatment with an anthracycline and a taxane. The primary objectives of the Phase I portion of this clinical trial are to determine the dose-limiting toxicities and maximum tolerated dose, and to assess the safety and tolerability of ispinesib administered as a 1-hour intravenous infusion on days 1 and 15 of a 28-day cycle. The secondary objectives are to characterize the pharmacokinetics of ispinesib on this schedule and to evaluate the effect of ispinesib on biomarkers of cell proliferation in patients with accessible tumors. In September 2008, at the American Society of Clinical Oncology Breast Cancer Symposium, we presented interim results from this trial. These data demonstrated that ispinesib was well-tolerated on this dosing schedule, with the most frequent adverse event being neutropenia. The best responses observed to date were investigator-reported tumor reductions of 30% or greater in the sum of the target lesion diameters, reported in 3 patients. One of these patients had an investigator-reported partial response according to the Response Evaluation Criteria in Solid Tumors. We presented additional data related to ispinesib at the San Antonio Breast Cancer Symposium in December 2008. We continue to enroll and dose-escalate patients in the Phase I portion of this trial.

Ispinesib with capecitabine: In June 2008, we announced the results of a Phase Ib clinical trial sponsored by GSK designed to evaluate ispinesib in combination with capecitabine, an oral chemotherapy agent commonly used in the treatment of breast cancer. The investigators in this clinical trial concluded that the combination of ispinesib with capecitabine had an acceptable tolerability profile on the 21-day schedule investigated in the trial. The dose-limiting toxicities in this combination regimen were consistent with the monotherapy toxicities of ispinesib (prolonged neutropenia) and capecitabine (rash). In this trial, the best response observed among the 24 patients treated was a partial response in a patient with advanced breast cancer. In addition, 11 patients had a response of stable disease.

Pediatric Solid Tumors: In June 2008, at the American Society of Clinical Oncology annual meeting, the NCI presented final data from a Phase I clinical trial designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of ispinesib as monotherapy administered to pediatric patients with relapsed or refractory solid tumors on days 1, 8 and 15 of a 28-day cycle. The authors concluded that the maximum tolerated

Table of Contents

dose on this schedule for this patient population was 9 mg/m². The best response observed was stable disease at 7 courses. Three patients experienced stable disease for longer than 3 courses of therapy. Ispinesib was well-tolerated, with neutropenia and hepatotoxicity representing the most commonly observed dose-limiting toxicities.

SB-743921

SB-743921 was studied by GSK in a dose-escalating Phase I clinical trial evaluating its safety, tolerability and pharmacokinetics in advanced cancer patients when administered intravenously on a once every 21-day schedule. The observed toxicities at the recommended Phase II dose were manageable. Dose-limiting toxicities 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 maximum tolerated dose. As a result of the expiration of GSK's option relating to SB-743921, we have retained all development and commercialization rights to SB-743921. We are conducting a Phase I/II clinical trial evaluating SB-743921 in patients with Hodgkin or non-Hodgkin lymphoma on a more dose-dense schedule than was previously evaluated by GSK. We intend to complete the Phase I portion of this trial. We intend to seek a strategic partner for the future development and commercialization of SB-743921.

Phase I/II Hodgkin and Non-Hodgkin Lymphoma: We are continuing to conduct the Phase I portion of a Phase I/II clinical trial of SB-743921. The primary objectives of the Phase I portion of this trial are to determine the dose-limiting toxicities and maximum tolerated dose and to assess the safety and tolerability of SB-743921 administered as a 1-hour intravenous infusion on days 1 and 15 of a 28-day cycle, a more dose-dense schedule than was previously evaluated, first without and then with the prophylactic administration of granulocyte colony-stimulating factor (G-CSF). The secondary objectives are to characterize the pharmacokinetics of SB-743921 administered on this schedule and to evaluate the effect of SB-743921 on biomarkers of cell proliferation in patients with accessible tumors. In 2008, we presented interim data from this trial at several scientific conferences, most recently at the December 2008 American Society of Hematology meeting. At this interim analysis point, 51 patients had been treated; all were evaluable for safety and 43 were evaluable for efficacy. The maximum tolerated dose of SB-743921 was 6 mg/m² when given days 1 and 15 every 28 days without prophylactic G-CSF support. This represents a greater dose density (0.43 mg/m²/day) than was achieved on the previously studied schedule; i.e., 4 mg/m² once every 21 days (0.19 mg/m²/day). The main dose-limiting toxicity observed without G-CSF was neutropenia; therefore, further dose escalation with empiric, prophylactic G-CSF was initiated and is ongoing. The trial is currently enrolling at 9 mg/m² with prophylactic G-CSF support. Grade 3 and 4 toxicities other than neutropenia were uncommon; in particular, no evidence of neuropathy or alopecia greater than Grade 1 have been observed. As of March 2009, three partial responses have been reported at doses at or above 6 mg/m², two in patients with Hodgkin lymphoma and one in a patient with non-Hodgkin lymphoma.

GSK-923295

GSK-923295, an inhibitor of CENP-E, is the third drug candidate to arise from our strategic alliance with GSK. CENP-E is directly involved in certain biological processes essential for cancer cells to proliferate. GSK-923295 causes partial and complete shrinkages of human tumors in animal models and has exhibited properties in these studies distinguishing it from ispinesib and SB-743921.

Phase I First-Time-in-Humans: During 2008, GSK continued to enroll patients and dose-escalate in an ongoing Phase I clinical trial of GSK-923295. The primary objective of this dose-escalation and pharmacokinetic Phase I clinical trial is to determine the maximum tolerated dose, dose-limiting toxicities, safety and pharmacokinetics of GSK-923295 in advanced, refractory solid tumors. Interim results from this trial were presented in October 2008 at the EORTC NCI-AACR International Symposium. GSK-923295 was well-tolerated at doses evaluated to date, ranging from 10 to 105 mg/m². Of the adverse events observed, nausea and fatigue (all less than or equal to Grade 2) were the most

frequent non-hematological toxicities. Anemia (all less than or equal to Grade 2) was the most frequent hematological toxicity. In addition, no neurotoxicity was observed. To date, the maximum tolerated dose has not been reached. One reversible dose-limiting toxicity was observed in the form of aspartate aminotransferase elevation. The plasma pharmacokinetics of GSK-923295 were dose-proportional and exhibited low intra-patient and modest inter-patient variability.

Table of Contents

Preclinical: At the October 2008 EORTC NCI-AACR International Symposium, GSK presented two posters containing preclinical data relating to GSK-923295. The first poster concluded that positron emission tomography using 2-[18F] fluoro-s-deoxy-d-glucose imaging may provide a means of evaluating pharmacodynamic activity in patients treated with GSK-923295. The second poster concluded that GSK-923295 has dose-dependent pharmacodynamic activity in Colo205 human xenografts.

We anticipate that GSK will initiate a Phase II clinical trial of GSK-923295 in 2009.

Research and Development Expense

Our research and development expense was \$54.0 million, \$53.4 million and \$49.2 million for 2008, 2007 and 2006, respectively, and \$337.4 million for the period from August 5, 1997 (date of inception) through December 31, 2008. Total operating expense was \$71.5 million, \$70.1 million and \$64.5 million for 2008, 2007 and 2006, respectively, and \$440.4 million for the period from date of inception through December 31, 2008.

Our Patents and Other Intellectual Property

Our policy is to seek patent protection for the technologies, inventions and improvements that we develop that we consider important to the advancement of our business. As of December 31, 2008, we had 127 issued U.S. patents and over 200 additional pending U.S. and foreign patent applications. In addition, we have an exclusive license from the University of California and Stanford University to 13 issued U.S. patents and an issued European patent. We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive position. Our commercial success will depend on obtaining and maintaining patent protection and trade secret protection for our drug candidates and technologies and our 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 cover them or we maintain them as trade secrets.

With regard to our oncology drug candidates currently in clinical trials, we have a U.S. patent covering ispinosib that will expire in 2020, unless extended, and a U.S. patent covering SB-743921 will expire in 2023, unless extended. However, both ispinosib and SB-743921 are still in clinical development and have not yet been approved by the FDA. If either of these drug candidates is approved, then pursuant to federal law, we may apply for an extension of the U.S. patent term for a patent covering the approved drug, which extension could extend the term of the applicable patent by up to a maximum of five additional years. We have U.S. and foreign patent applications pending for GSK-923295. At present, it is not known or determinable whether patents will issue from any of these applications or what the expiration dates would be for any patents that do issue.

With regard to our drug candidates directed to muscle biology targets, we have U.S. and foreign patent applications pending for each of our drug candidates and potential drug candidates. We have received a notice of patent allowance from the U.S. Patent and Trademark Office for a patent relating to our cardiac muscle myosin activators. It is not known or determinable whether other patents will issue from any of our other pending applications or what the expiration dates would be for any patents that do issue.

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. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the claim scope of these patents, our ability to enforce our existing patents and to obtain and enforce patents that may issue from any pending or future patent applications is uncertain and involves complex legal, scientific and factual questions. The standards which the U.S. Patent and Trademark Office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and are subject to change. To date, no consistent policy has emerged regarding the breadth of

claims allowed in biotechnology and pharmaceutical patents. Thus, we cannot be sure that any patents will issue from any pending or future patent applications owned by or licensed to us. Even if patents do issue, we cannot be sure that the claims of these patents will be held valid or enforceable by a court of law, will

Table of Contents

provide us with any significant protection against competitive products, or will afford us a commercial advantage over competitive products. 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 the inventions covered by our pending patent applications and issued patents;

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 or the claims that issue may be narrow in scope and not provide us with competitive advantages;

our and our licensors issued patents may not provide a basis for commercially viable drugs or therapies 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 that may result in a reduction in their scope or their loss altogether;

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.

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

Our ability to commercialize drugs depends on our ability to use, manufacture and sell those drugs without infringing the patents or other proprietary rights of third parties. U.S. and foreign issued patents and pending patent applications owned by third parties exist that may be relevant to the therapeutic areas and chemical compositions of our drug candidates and potential drug candidates. While we are aware of certain relevant patents and patent applications owned by third parties, there may be issued patents or pending applications of which we are not aware that could cover our drug candidates. Because patent applications are often not published immediately after filing, there may be currently pending applications, unknown to us, which could later result in issued patents that our activities with our drug candidates could infringe.

Currently, we are aware of an issued U.S. patent and at least one pending U.S. patent application assigned to Curis, Inc. (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 quinazolinone 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. Two of the Australian applications have been allowed and two of the European applications have been granted. We have opposed the granting of certain of these patents to Curis in Europe and in Australia. Curis has withdrawn one of the Australian applications. 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 its licensee may assert that the manufacture, use, importation or sale of ispinesib may infringe one or more of these patents. We believe that we have valid defenses against the issued U.S. patent owned by Curis if it were to be asserted against us. However, we cannot guarantee that a court would find these 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 seek a license to these patents, we cannot guarantee that such a license would be available on acceptable terms, if at all.

The development of our drug candidates and the commercialization of any resulting drugs may be impacted by patents of companies engaged in competitive programs with significantly greater resources. This could result in the expenditure of significant legal fees and management resources.

Table of Contents

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 often difficult to protect, especially outside of the United States. 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. Even if we are able to maintain our trade secrets as confidential, our competitors may independently develop information that is equivalent or similar to our trade secrets.

We seek to protect our intellectual property by requiring our employees, consultants, contractors and other advisors 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 preclude 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.

For further details on the risks relating to our intellectual property, please see the risk factors under Item 1A of this report, including, but not limited to, the risk factors entitled "Our success depends substantially upon our ability to obtain and maintain intellectual property protection relating to our drug candidates and research technologies" and "If we are sued for infringing third party intellectual property rights, it will be costly and time-consuming, and an unfavorable outcome would have a significant adverse effect on our business."

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 regulations;

- submission to the FDA of an IND, which must become effective before clinical trials may begin;

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

- submission of a new drug application (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 practice (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, and 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 period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects may 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

Table of Contents

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 (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, the IRB or their foreign equivalents, 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 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: These 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 conduct 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 conduct 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, known as Phase IV clinical trials.

The Food and Drug Amendments Act of 2007 generally requires that the clinical trials we conduct for our drug candidates, both before and after approval, and the results of those trials, be included in a clinical trials registry database that is available and accessible to the public via the internet. A failure by us to properly participate in the clinical trial database registry could subject us to significant civil monetary penalties.

Health care providers in the United States, including research institutions from which we or our partners obtain patient information, are subject to privacy rules under the Health Insurance Portability and Accountability Act of 1996 and state and local privacy laws. In the European Union, these entities are subject to the Directive 95/46-EC of the European Parliament on the protection of individuals with regard to the processing of personal data and individual European Union member states implementing additional legislation. Other countries have similar privacy legislation. We could face substantial penalties if we knowingly receive individually identifiable health information from a health

care provider that has not satisfied the applicable privacy laws. In addition, certain privacy laws and genetic testing laws may apply directly to our operations and/or those of our partners and may impose restrictions on the use and dissemination of individuals' health information and use of biological samples.

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

Table of Contents

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 often, but not always, follows the advisory board's 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 or impose other conditions that must be met in order to secure final approval for an NDA. 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 partners 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.

Satisfaction of FDA regulations and requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years. The actual time required may vary substantially based upon the type, complexity and novelty of the drug candidate 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 future U.S. or foreign governmental regulations may be implemented.

Other regulatory requirements. Any drugs manufactured or distributed by us or our partners pursuant to FDA approvals or their foreign counterparts are subject to continuing regulation by the applicable regulatory authority, 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 other applicable regulatory authorities, and are subject to periodic unannounced inspections by these regulatory authorities 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 and other regulatory requirements. If our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA or its foreign counterparts may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug.

For further details on the risks relating to government regulation of our business, please see the risk factors under Item 1A of this report, including, but not limited to, the risk factor entitled "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."

Competition

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address cardiovascular diseases and other diseases relating to muscle dysfunction and cancer, each of which is highly competitive. We face significant competition from most pharmaceutical companies and biotechnology companies

Table of Contents

that are also researching and selling products designed to address cardiovascular diseases, diseases and medical conditions associated with skeletal muscle weakness and wasting, 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, diseases where there is muscle dysfunction, 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 selection of suitable indications for which to develop our drug candidates;
- the successful completion of clinical development and laboratory testing of our drug candidates;
- the timing and scope of any regulatory approvals we or our partners obtain for our drug candidates;
- our or our partners' ability to manufacture and sell commercial quantities of our approved drugs to meet market demand;
- 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 current or future competitors may also commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates. These organizations also compete with us to attract qualified personnel and potential parties for acquisitions, joint ventures or other strategic alliances.

If CK-1827452 is approved for marketing by the FDA for heart failure, that compound would compete against current generically available therapies, such as milrinone, dobutamine or digoxin or newer branded drugs such as nesiritide, and potentially against other drug candidates in development. 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 would compete against existing cancer treatments such as paclitaxel (and its generic equivalents), docetaxel, vincristine, vinorelbine, navelbine, ixabepilone and potentially against other 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 other companies are conducting research and development focused on KSP and other mitotic kinesins, and other approaches to inhibiting mitosis.

For further details on the risks relating to government regulation of our business, please see the risk factors under Item 1A of this report, including, but not limited to, the risk factor entitled Our competitors may develop drugs that are less expensive, safer or more effective than ours, which may diminish or eliminate the commercial success of any drugs that we may commercialize.

Table of Contents

Employees

As of December 31, 2008, our workforce consisted of 110 full-time employees, 30 of whom hold Ph.D. or M.D. degrees, or both, and 23 of whom hold other advanced degrees. Of our total workforce, 81 are engaged in research and development and 29 are engaged in business development, finance and administration functions.

In September 2008, we announced a restructuring plan to realign our workforce and operations in line with a strategic reassessment of our research and development activities and corporate objectives. As a result, we have focused our research activities to our muscle contractility programs while continuing our ongoing clinical trials in heart failure and cancer and discontinued early research activities directed to oncology. To implement this plan, we reduced our workforce by approximately 29%, or 45 employees, to 112 employees. The affected employees were provided with severance payments and outplacement assistance.

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 (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 100 F Street, NE, 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 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 these risk factors to be a complete statement of all the potential risks or uncertainties that we face.

Risks Related To Our Business

We will need substantial additional capital in the future to sufficiently fund our operations.

We have consumed substantial amounts of capital to date, and our operating expenditures will increase over the next several years if we expand our research and development activities. We have funded all of our operations and capital expenditures with proceeds from private and public sales of our equity securities, strategic alliances with GSK, Amgen and others, equipment financings, interest on investments and government grants. We believe that our existing cash and cash equivalents, short-term investments, interest earned on investments, proceeds from our loan with UBS Bank USA and proceeds from our 2007 committed equity financing facility with Kingsbridge should be sufficient to

meet our projected operating requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of our drug candidates and other research and development activities, including risks and uncertainties that could impact the rate of progress of our development activities, we are unable to estimate with certainty the amounts of capital outlays and operating expenditures associated with these activities.

Table of Contents

For the foreseeable future, our operations will require significant additional funding, in large part due to our research and development expenses and the absence of any revenues from product sales. Until we can generate a sufficient amount of product revenue, we expect to raise future capital through public or private equity offerings, debt financings and strategic alliance and licensing arrangements. We do not currently have any commitments for future funding other than milestone and royalty payments that we may receive under our collaboration and license agreement with GSK and, if Amgen exercises its option with respect to CK-1827452, option fees and milestone and royalty payments that we may receive under our collaboration and option agreement with Amgen. We may not receive any further funds under either of these agreements. Our ability to raise funds may be adversely impacted by current economic conditions, including the effects of the recent disruptions to the credit and financial markets in the United States and worldwide. In particular, the pool of third-party capital that in the past has been available to development-stage companies such as ours has decreased significantly in recent months, and such decreased availability may continue for a prolonged period. As a result of these and other factors, we do not know whether additional financing will be available when needed, or that, if available, such financing would be on terms favorable to our stockholders or us.

To the extent that we raise additional funds by issuing equity securities, our stockholders will 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, the financing may involve covenants that restrict our business activities. In addition, such funding, if needed, may not be available to us on favorable terms, or at all.

If we can not raise the funds we need to operate our business, we will need to discontinue certain research and development activities and our stock price likely would be negatively affected.

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.

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. 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 expect to incur increasing losses for at least several more 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 in the United States and other regulatory authorities 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 any 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 potential treatment of heart failure, and ispinesib, SB-743921 and GSK-923295, our drug candidates for the potential treatment of cancer, are currently our only drug candidates in clinical trials. We cannot be 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 clinical testing or commercialization. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially marketed for several years, if at all. The

Table of Contents

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.

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 adequately demonstrate to the FDA and foreign regulatory authorities that the drug candidate is sufficiently safe and effective with substantial evidence from well-controlled clinical trials. In clinical trials we will need to demonstrate efficacy for the treatment of specific indications and monitor safety throughout the clinical development process and possibly following approval. None of our drug candidates have yet been demonstrated to be safe and effective in clinical trials and they may never be. In addition, for each of our current preclinical compounds, we must adequately demonstrate satisfactory chemistry, formulation, stability and toxicity in order to submit an IND to the FDA, or an equivalent application in foreign jurisdictions, that would allow us to advance that compound into clinical trials. If our current or future preclinical studies or clinical trials are unsuccessful, our business 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 adequately support the filing of an IND (or a foreign equivalent) with respect to our potential drug candidates. Even if these applications are 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, for any of our drug candidates, the results from Phase I clinical trials in healthy volunteers and clinical results from Phase I and II trials in patients are not necessarily indicative of the results of larger Phase III clinical trials that are necessary to establish whether the drug candidate is safe and effective for the applicable indication.

In addition, the clinical trials for any of our drug candidates may not be designed with focus on the appropriate indications, tumor types, patient populations, dosing regimens, safety or efficacy parameters or other variables to provide the necessary safety or efficacy data to support regulatory approval to commercialize the resulting drugs. 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, the methods we select to assess particular safety or efficacy parameters may not yield the same statistical precision in estimating our drug candidates' effects as may other alternative methodologies. Even if we believe the data collected from clinical trials of our drug candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these 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 observed in preclinical studies for some compounds in a particular research and development program may also 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 itself or from impurities or degradants that are present in the active pharmaceutical ingredient or could form over time in the formulated drug candidate or the active pharmaceutical ingredient. These toxicities or adverse effects could delay or prevent the filing of an IND (or a foreign equivalent) with respect to our drug candidates or potential drug candidates or cause us to cease clinical trials with respect to any drug candidate. If these or other adverse effects are severe or frequent enough to outweigh the potential efficacy of a drug candidate, the FDA or other regulatory authorities could deny approval of that drug candidate for any or all targeted indications. The FDA, other regulatory

authorities, our partners or we may suspend or terminate clinical trials with our drug candidates at any time. Even if one or more of our drug candidates were approved for sale as drugs, 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 those drugs. Indications of potential adverse effects or toxicities

Table of Contents

which do not seem significant during the course of clinical trials may later turn out to actually constitute serious adverse effects or toxicities when a drug is used in large populations or for extended periods of time.

We have observed certain adverse effects in the clinical trials conducted with our drug candidates. For example, in clinical trials of ispinesib, the most commonly observed 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.

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 resulting drugs, may significantly harm our business and negatively affect our stock price.

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

Clinical trials are subject to rigorous regulatory requirements and are very expensive, difficult and time-consuming to design and implement. The length of time and number of trial sites and patients required for clinical trials vary substantially based on the type, complexity, novelty, intended use of the drug candidate and safety concerns. We estimate that the clinical trials of our current drug candidates will each continue for several years. However, the clinical trials for all or any of these drug candidates 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;

delays or additional costs in developing, or inability to develop, appropriate formulations of our drug candidates for clinical trial use, including an appropriate modified release formulation for CK-1827452;

slower than expected rates of patient recruitment and enrollment, including as a result of competition for patients with other clinical trials; limited numbers of patients that meet the enrollment criteria; patients, investigators or trial 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 or its foreign equivalent may require changes to a protocol that then require approval from regulatory agencies and other IRBs and their foreign equivalents, or regulatory authorities may require changes to a protocol that then require approval from the IRBs or their foreign equivalents;

for clinical trials conducted in foreign countries, the time and resources required to identify, interpret and comply with foreign regulatory requirements or changes in those requirements, and political instability or natural disasters occurring in those countries;

lack of effectiveness of our drug candidates during clinical trials;

unforeseen safety issues;

inadequate supply of clinical trial materials;

Table of Contents

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;

failure by us, our clinical research organizations, investigators or site personnel to comply with good clinical practices and other applicable laws and regulations;

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, to the extent we elect to develop a drug candidate without a strategic partner, we will need to expand our development capabilities and will require additional funding.

The development of drug candidates is complicated and expensive, and we currently have limited financial and operational resources to carry out drug development. In order to expand our capability to conduct clinical development we will need to bring additional skills, technical expertise and resources into our organization, which will require significant additional funding.

Pursuant to our collaboration and option agreement with Amgen, we are responsible for conducting Phase IIa clinical development for our drug candidate CK-1827452. We cannot engage another strategic partner for CK-1827452, except in Japan, until Amgen elects not to exercise its option to conduct later-stage clinical development for CK-1827452 or its option expires, whichever is earlier. We intend to initiate a Phase IIb clinical trial for CK-1827452 regardless of whether Amgen exercises its option, which will require significant operational and financial resources.

We have retained all rights to develop and commercialize isspinesib and SB-743921. We currently do not have a strategic partner for these drug candidates. Currently, we are conducting the Phase I portion of a Phase I/II clinical trial for each of isspinesib in breast cancer and SB-743921 in Hodgkin and non-Hodgkin lymphoma. We intend to complete the Phase I portion of each of these clinical trials. We rely on GSK to conduct preclinical and clinical development for GSK-923295 in cancer. If GSK elects to terminate its development activities with respect to GSK-923295, we currently do not have an alternative strategic partner for this drug candidates.

We intend to seek strategic partners or other third party sources of funding for the future development and commercialization of isspinesib and SB-743921, for CK-1827452 if Amgen does not exercise its option and for GSK-923295 should GSK terminate its development activities. We may be unable to enter into an agreement with a third party that would provide sufficient operational support and funding for the further clinical development of these drug candidates on acceptable terms, or at all. In that case, we would have to curtail or abandon development of one or more of these drug candidates.

If we fail to enter into and maintain successful strategic alliances for our drug candidates, potential drug candidates or research and development programs, we will have to reduce, delay or discontinue our advancement

of those drug candidates, potential drug candidates and programs or increase our expenditures.

Our strategy for developing, manufacturing and commercializing 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. We currently have strategic alliances with Amgen relating to CK-1827452 and with GSK relating to GSK-923295. Similarly, we expect to rely on one or more strategic partners to advance and develop ispinesib and SB-743921 and our potential drug candidates directed towards skeletal sarcomere and smooth muscle contractility. However, we may not be able to negotiate and enter into such strategic alliances on acceptable terms, if at all. If we are not able to

Table of Contents

maintain our existing strategic alliances or establish and maintain additional strategic alliances, we will have to limit the size or scope of, or delay or discontinue, one or more of our drug development programs or research programs, or undertake and fund these programs ourselves. If we elect to continue to conduct any of these drug development programs or research programs on our own, we will need to obtain significant additional capital, which may not be available to us on acceptable terms or at all.

If Amgen does not exercise its option for CK-1827452, we will have to reduce, delay or discontinue our development of CK-1827452 or increase our expenditures.

Our collaboration and option agreement with Amgen grants it an option to obtain an exclusive license for the development and commercialization rights for CK-1827452 world-wide, except 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 certain Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed development plan, the results of which reasonably support its progression into Phase IIb clinical development. We believe we have completed delivery of this data to Amgen, which can exercise its option by paying us a specified option fee within the pre-defined option exercise period.

Amgen may elect not to exercise its option, irrespective of the data that we provide, may dispute whether we have provided sufficient information and data to require it to decide whether to exercise its option, or may seek to require us to conduct additional clinical trial activities prior to deciding whether to exercise its option. If Amgen elects not to exercise its option for CK-1827452, we would have to seek an alternative strategic partner for the CK-1827452 development program. However, we may not be able to negotiate and enter into such a strategic alliance on acceptable terms, if at all. Without a strategic partner, we would have to limit the size or scope of, or delay or discontinue, development of CK-1827452 or undertake and fund that development ourselves. If we elect to continue to conduct development on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. Further, a decision by Amgen not to exercise its option could negatively affect our stock price.

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. 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. We do not control the clinical development being conducted or that may be conducted in the future by GSK, including the timing of initiation, termination or completion of clinical trials, the analysis of data arising out of those clinical trials or the timing of release of data concerning those clinical trials, which may impact our ability to report on GSK's results.

If the initial results of one or more 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 that time is relatively small. If GSK abandons GSK-923295, it would result in a

delay in or could prevent us from commercializing GSK-923295, and would delay and could prevent us from obtaining revenues for this drug candidate. 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

Table of Contents