

CYTOKINETICS INC
Form 424B5
February 19, 2014
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-192125

This preliminary prospectus supplement and the accompanying prospectus relate to an effective registration statement under the Securities Act of 1933, as amended, but the information in this prospectus supplement is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated February 19, 2014

PROSPECTUS SUPPLEMENT

(To the Prospectus dated December 23, 2013)

Shares

Common Stock

We are offering shares of our common stock pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is listed on The NASDAQ Capital Market under the symbol CYTK. The last reported sale price of our common stock on February 18, 2014 was \$9.74 per share.

Our business and an investment in our common stock include significant risks. See Risk Factors beginning on page S-4 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
	\$	\$
Public offering price		
Underwriting discount(1)		
Proceeds, before expenses, to us		

(1) See Underwriting beginning on page S-25 for a description of the compensation payable to the underwriters. The underwriters may also purchase up to an additional shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover overallocments, if any. If the underwriters exercise the option in full, the total discount will be \$ and the total net proceeds, before expenses, to us will be \$.

The underwriters expect to deliver the shares against payment on or about February , 2014.

Cowen and Company

Sole Book-Running Manager

JMP Securities

Lead Manager

February , 2014.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

	Page
<u>About this Prospectus Supplement</u>	S-ii
<u>Forward-Looking Statements</u>	S-iii
<u>Prospectus Supplement Summary</u>	S-1
<u>Risk Factors</u>	S-4
<u>Use of Proceeds</u>	S-23
<u>Dividend Policy</u>	S-23
<u>Dilution</u>	S-24
<u>Underwriting</u>	S-25
<u>Legal Matters</u>	S-29
<u>Experts</u>	S-29
<u>Where You Can Find More Information</u>	S-29
<u>Incorporation of Certain Information by Reference</u>	S-30

Prospectus

	Page
<u>Prospectus Summary</u>	2
<u>Risk Factors</u>	5
<u>Disclosure Regarding Forward-Looking Statements</u>	5
<u>Use of Proceeds</u>	7
<u>Ratio of Earnings to Combined Fixed Charges and Preference Security Dividends</u>	8
<u>Description of Capital Stock</u>	8
<u>Description of the Warrants</u>	10
<u>Plan of Distribution</u>	13
<u>Legal Matters</u>	14
<u>Experts</u>	14
<u>Where You Can Find More Information</u>	14
<u>Information Incorporated by Reference</u>	14

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated December 23, 2013, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date will modify or supersede the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement titled **Where You Can Find More Information** and **Incorporation of Certain Information by Reference**.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement to Cytokinetics, we, us, our or similar references mean Cytokinetics, Incorporated, unless the context requires otherwise.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Table of Contents

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about or relating to:

our expected cash, cash equivalents and investments as of December 31, 2013;

guidance concerning revenues, research and development expenses and general and administrative expenses for 2014;

our capital requirements and needs for additional financing;

the initiation, design, conduct, enrollment, progress, timing and scope of clinical trials and development activities for our drug candidates conducted by ourselves or our partners, Amgen, Inc. (Amgen) and Astellas Pharma Inc. (Astellas) including the anticipated timing for initiation of clinical trials, anticipated rates of enrollment for clinical trials and anticipated timing of results becoming available or being announced from clinical trials;

the results from the clinical trials and non-clinical and preclinical studies of our drug candidates and other compounds, and the significance and utility of such results;

the ability of our amendments to the protocol of our BENEFIT-ALS clinical trial to maintain the originally intended statistical power of the trial;

our and our partners' plans or ability to conduct the continued research and development of our drug candidates and other compounds;

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

the properties and potential benefits of, and the potential market opportunities for, our drug candidates and other compounds, including the potential indications for which they may be developed;

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

our receipt of milestone payments, royalties, reimbursements and other funds from current or future partners under strategic alliances, such as with Amgen or Astellas;

our ability to continue to identify additional potential drug candidates that may be suitable for clinical development;

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

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

the utility of our focus on the biology of muscle function, and our ability to leverage our experience in muscle contractility to other muscle functions;

our ability to protect our intellectual property and to avoid infringing the intellectual property rights of others;

S-iii

Table of Contents

expected future sources of revenue and capital;

losses, costs, expenses and expenditures;

future payments under loan and lease obligations;

the expected recognition of revenue under our collaboration agreements;

potential competitors and competitive products;

retaining key personnel and recruiting additional key personnel;

expected timing for recognition of compensation cost related to unvested stock options; and

the potential impact of recent accounting pronouncements on our financial position or results of operations. Such forward-looking statements involve risks and uncertainties, including, but not limited to:

the expected amount of our cash, cash equivalents and investments as of December 31, 2013 is preliminary, has not been audited and is subject to change upon completion of our ongoing audit;

our ability to acquire the funding necessary to conduct the one or more confirmatory Phase III clinical trials for tirasemtiv in patients with amyotrophic lateral sclerosis (also known as ALS or Lou Gehrig's disease) that we expect will be required to obtain marketing approval for tirasemtiv for the treatment of ALS;

decisions by Amgen with respect to the timing, design and conduct of research and development activities for omecamtiv mecarbil and other related compounds, including decisions to postpone or discontinue research or development activities relating to omecamtiv mecarbil and other related compounds;

decisions by Astellas with respect to the timing, design and conduct of research and development activities for CK-2127107 and other skeletal muscle activators, including decisions to postpone or discontinue research or development activities relating to CK-2127107 and other skeletal muscle activators;

our ability to enter into strategic partnership agreements for any of our programs on acceptable terms and conditions or in accordance with our planned timelines;

our ability to obtain additional financing on acceptable terms, if at all;

our receipt of funds and access to other resources under our current or future strategic alliances;

difficulties or delays in the development, testing, manufacturing or commercialization of our drug candidates;

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

difficulties or delays in the manufacture and supply of clinical trial materials;

failure by our contract research organizations, contract manufacturing organizations and other vendors to properly fulfill their obligations or otherwise perform as expected;

results from non-clinical studies that may adversely impact the timing or the further development of our drug candidates and other compounds;

S-iv

Table of Contents

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;

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

difficulties or delays in achieving market access and reimbursement for our drug candidates and the potential impacts of health care reform;

changes in laws and regulations applicable to drug development, commercialization or reimbursement;

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

potential infringement or misuse by us of the intellectual property rights of third parties;

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

potential ownership changes under Internal Revenue Code Section 382; and

the timeliness and accuracy of information filed with the SEC by third parties.

In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, plans, anticipates, believes, estimates, projects, predicts, potential and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading Risk Factors on page S-4 of this prospectus supplement and in our SEC filings. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement.

You should read this prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

You should rely only on the information contained, or incorporated by reference, in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering. We and the underwriters for this offering have not authorized anyone to provide you with different information. The common stock offered under this prospectus is not being offered in any jurisdiction where the offer

is not permitted. You should not assume that the information contained in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date on the front of this prospectus supplement or the accompanying prospectus, as applicable, or that any information incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date of the document so incorporated by reference. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

S-v

Table of Contents**PROSPECTUS SUPPLEMENT SUMMARY**

*This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information under the heading *Risk Factors* in this prospectus supplement on page S-4.*

Cytokinetics, Incorporated**Our Business**

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 most advanced research and development programs relate to the biology of muscle function and are directed to small molecule modulators of the contractility of skeletal or cardiac muscle. We are also conducting earlier-stage research directed to other compounds with the potential to modulate muscle contractility and other muscle functions, such as growth, energetics and metabolism.

Our lead drug candidate from our skeletal muscle contractility program, tirasemtiv (formerly known as CK-2017357), is a fast skeletal muscle troponin activator. Cytokinetics holds the rights to tirasemtiv and is independently developing this drug candidate for the potential treatment of ALS and other neuromuscular disorders. We are currently conducting a Phase II clinical trials program for tirasemtiv, including an ongoing Phase IIb clinical trial in patients with ALS, known as BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with Tirasemtiv in ALS). We have concluded enrollment in BENEFIT-ALS and we anticipate reporting results from this clinical trial in April 2014. Tirasemtiv has been granted orphan drug designation and fast track status by the FDA and orphan medicinal product designation by the European Medicines Agency, in each case for the potential treatment of ALS. We anticipate that we will need to conduct at least one confirmatory Phase III clinical trial of tirasemtiv in patients with ALS to gain marketing approval.

We are also developing CK-2127107, a structurally distinct, fast skeletal muscle troponin activator, under a strategic alliance with Astellas established in June 2013. CK-2127107 is being evaluated in Phase I clinical trials for potential non-neuromuscular indications associated with muscle weakness. We also are conducting joint research with Astellas directed to next-generation skeletal muscle activators.

Our lead drug candidate from our cardiac muscle contractility program, omecamtiv mecarbil (formerly known as CK-1827452), is a novel cardiac muscle myosin activator that is being developed under a strategic alliance with Amgen. In June 2013, we expanded the collaboration to include Japan. As a result, Amgen holds an exclusive license to develop and commercialize omecamtiv mecarbil worldwide, subject to our development and commercialization participation rights. An intravenous formulation of omecamtiv mecarbil was studied in a Phase IIb clinical trial known as ATOMIC-AHF (Acute Treatment with Omecamtiv Mecarbil to Increase Contractility in Acute Heart Failure), which was designed to evaluate the safety and efficacy of omecamtiv mecarbil in patients with left ventricular systolic dysfunction who are hospitalized with acute heart failure. Another Phase II clinical trial, known as COSMIC-HF

(Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure), is being conducted. The primary objectives of this trial are selecting an oral modified release formulation and doses of omecamtiv mecarbil for chronic twice-daily dosing in patients with heart failure and left ventricular systolic dysfunction, and characterizing its pharmacokinetics during 20 weeks of treatment. We also are conducting joint research with Amgen directed to next-generation compounds in our cardiac muscle contractility program.

Two of our drug candidates have demonstrated pharmacodynamic activity in patients: tirasemtiv in patients with ALS, in patients with myasthenia gravis and in patients with claudication associated with peripheral artery disease; and omecamtiv mecarbil in patients with heart failure. Our drug candidate CK-2127107 has demonstrated pharmacological activity in preclinical models. In 2014, we expect to continue to focus on translating the observed pharmacodynamic activity of these compounds into potentially meaningful clinical benefits for patients.

S-1

Table of Contents

Financial Update

While we have not finalized our full financial results for the fiscal year ended December 31, 2013, we expect to report that we had approximately \$80.2 million of cash, cash equivalents and investments as of December 31, 2013. This amount is preliminary, has not been audited and is subject to change upon completion of our ongoing audit. Additional information and disclosures would be required for a more complete understanding of our financial position and results of operations as of December 31, 2013.

Corporate Information

We were incorporated in Delaware in August 1997. We conduct our administration, finance, business development, research and clinical development, commercial development, quality assurance and regulatory affairs activities primarily from our headquarters located at 280 East Grand Avenue, South San Francisco, CA. Our general telephone number at that address is (650) 624-3000 and our website is located at www.cytokinetics.com. The information on, or that can be accessed through, our website is not incorporated by reference in this prospectus supplement, and you should not consider it to be a part of this prospectus supplement or the accompanying prospectus.

Table of Contents

The Offering

Common stock offered by us	shares
Overallotment option	shares
Common stock to be outstanding immediately after this offering	shares
Use of proceeds	We intend to use the net proceeds from this offering for research and development and general corporate purposes, including working capital. See Use of Proceeds on page S-23 of this prospectus supplement.
Risk factors	Investing in our common stock involves significant risks. See Risk Factors on page S-4 of this prospectus supplement.
Listing	Our common stock is listed on The NASDAQ Capital Market under the symbol CYTK.
The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 29,503,123 shares outstanding as of September 30, 2013, and excludes as of that date:	

7,692,096 shares of common stock issuable upon the exercise of warrants outstanding, having a weighted average exercise price of \$5.95 per share;

2,451,522 shares of common stock issuable upon the exercise of stock options outstanding, having a weighted average exercise price of \$15.18 per share;

41,663 units of restricted stock outstanding; and

An aggregate of 2,357,486 shares of common stock reserved for future issuance under our stock option and employee stock purchase plans.

In addition, the number of shares of our common stock to be outstanding immediately after this offering as shown above excludes 1,534,686 shares of common stock that were sold subsequent to September 30, 2013 pursuant to an At-the-Market Issuance Sales Agreement that we entered into with McNicoll, Lewis & Vlask LLC on June 10, 2011.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their overallotment option.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flows could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related To Our Business

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 generally 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 all in early and mid-stage clinical testing, and we and our partners must conduct significant additional clinical trials before we and our partners 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 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 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 Amgen, Astellas and others, equipment financings, interest on investments and government grants. We believe that our existing cash and cash equivalents, short-term investments and interest earned on investments 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.

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. For example, we anticipate that we will need to conduct at least one Phase III clinical trial for tirasemtiv following the BENEFIT-ALS trial in order to obtain marketing approval for tirasemtiv for the potential treatment of ALS. We will require significant additional funding to enable us to conduct any such Phase III clinical trials. Until we can generate a sufficient amount of product revenue, we expect to raise future capital through strategic alliance and licensing arrangements, public or private equity offerings and debt financings. We do not currently have any commitments for future funding other than reimbursements, milestone and royalty payments that we may receive under our collaboration agreements with Amgen and Astellas. We may not receive any further funds under that agreement. Our ability to raise funds may be adversely impacted by current economic conditions. 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 through strategic alliances or licensing and other arrangements with third parties, 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 by issuing equity securities, our stockholders will experience additional dilution and our share price may decline. To the extent that we raise additional funds through debt financing, the financing may involve covenants that restrict our business activities. In addition, funding from any of these sources, if needed, may not be available to us on favorable terms, or at all, or in accordance with our planned timelines.

If we cannot raise the funds we need to operate our business, we will need to delay or discontinue certain research and development activities. For example, if we cannot raise the funds necessary to enable the conduct of the one or more Phase III clinical trials for tirasemtiv for the potential treatment of ALS that we anticipate will be required for marketing approval, our ability to complete the development of tirasemtiv will be delayed or suspended. If we delay or discontinue research and development activities, our stock price may be negatively affected.

S-4

Table of Contents

We have never generated, and may never generate, revenues from commercial sales of our drugs and we will 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 develop or obtain approval to market any drugs. To receive marketing approval for any drug candidate, we must demonstrate that the drug candidate satisfies 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. Currently, our only drug candidates in clinical development are omecamtiv mecarbil for the potential treatment of heart failure, tirasemtiv for the potential treatment of ALS and other neuromuscular disorders and CK-2127107 for the potential treatment of non-neuromuscular indications associated with muscle weakness. We cannot be certain that the clinical development of these or any future drug candidates will be successful, that they will receive the regulatory approvals required to commercialize them, that they will ultimately be accepted by prescribers or reimbursed by insurers 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 at least several years, if at all. The development of any one or all of these drug candidates may be discontinued at any stage of our clinical trials programs and we may not generate revenue from any of these drug candidates.

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 or our partners must adequately demonstrate to the satisfaction of FDA and foreign regulatory authorities that the drug candidate is sufficiently safe and effective with substantial evidence from well-controlled clinical trials. We or our partners will need to demonstrate efficacy in clinical trials for the treatment of specific indications and monitor safety throughout the clinical development process and 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 preclinical compounds, we or our partners must adequately demonstrate satisfactory chemistry, formulation, stability and toxicity in order to submit an investigational new drug application (IND) to the FDA, or an equivalent application in foreign jurisdictions, that would allow us to advance that compound into clinical trials. Furthermore, we or our partners may need to submit separate INDs (or foreign equivalent) to different divisions within the FDA (or foreign regulatory authorities) in order to pursue clinical trials in different therapeutic areas. Each new IND (or foreign equivalent) must be reviewed by the new division before the clinical trial under its jurisdiction can proceed, entailing all the risks of delay inherent to regulatory review. If our or our partners' 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 the results of preclinical studies for a drug candidate are sufficient to support such a filing, the results of preclinical studies do not necessarily predict the results of clinical trials. As an example, because the physiology of animal species used in preclinical studies may vary substantially from other animal species and from humans, it may be difficult to assess with certainty whether a finding from a study in a particular animal species will result in similar findings in other animal species or in humans. 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. Likewise, interim results from a clinical trial may not be indicative of the final results from that trial.

In addition, while the clinical trials of our drug candidates are designed based on the available relevant information, such information may not accurately predict what actually occurs during the course of the trial itself, which may have consequences for the conduct of an ongoing clinical trial or for the eventual results of that trial. For example, the number of patients planned to be enrolled in a placebo-controlled clinical trial is determined in part by estimates relating to expected treatment effect and variability about the primary endpoint. These estimates are based upon earlier nonclinical and clinical studies of the drug candidate itself and clinical trials of other drugs thought to have similar effects in a similar patient population. If information gained during the conduct of the trial shows these estimates to be inaccurate, we may elect to adjust the enrollment accordingly, which may cause delays in completing the trial, additional expense or a statistical penalty to apply to the evaluation of the trial results.

S-5

Table of Contents

Furthermore, in view of the uncertainties inherent in drug development, such clinical trials may not be designed with focus on indications, patient populations, dosing regimens, safety, efficacy or pharmacokinetic parameters or other variables that will provide the necessary safety or efficacy data to support regulatory approval to commercialize the resulting drugs. Clinical trials of our drug candidates are designed based on guidance or advice from regulatory agencies, which is subject to change during the development of the drug candidate at any time. Such a change in a regulatory agency's guidance or advice may cause that agency to deem results from trials to be insufficient to support approval of the drug candidate and require further clinical trials of that drug candidate to be conducted. In addition, individual patient responses to the dose administered of a drug may vary in a manner that is difficult to predict. Also, the methods we select to assess particular safety, efficacy or pharmacokinetic parameters may not yield the same statistical precision in estimating our drug candidates' effects as may other 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 from us or our partners, 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, our partners or the FDA or foreign regulatory authorities to modify, suspend or terminate clinical trials with respect to any drug candidate at any time during the development program. Further, the administration of two or more drugs contemporaneously can lead to interactions between them, and our drug candidates may interact with other drugs that trial subjects are taking. For example, in a Phase I drug-drug interaction study of tirasemtiv administered orally to healthy volunteers, co-administration of tirasemtiv and riluzole (an approved treatment for ALS) approximately doubled the average maximum riluzole plasma level, although it also appeared to reduce the variability of the riluzole plasma levels of the study subjects. If the 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. 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 or foreign regulatory authorities to impose restrictions on, or stop, the further marketing of those drugs. Indications of potential adverse effects or toxicities 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 Phase II clinical trials of tirasemtiv, adverse events of dizziness, fatigue, headache, somnolence (sleepiness), euphoric mood, muscle spasms, gait disturbance, pain in extremity, feeling drunk, blurred vision, muscular weakness, nausea, balance disorder, asthenia (loss of strength and energy), abnormal coordination and dysarthria (difficulty speaking) occurred more frequently during treatment with tirasemtiv than with placebo, with a possible trend for their frequencies to increase with increasing doses of tirasemtiv. In clinical trials of omecamtiv mecarbil, dose-limiting effects 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 the MB fraction of creatine kinase and cardiac troponins I and T, which are indicative of myocardial infarction.

In addition, clinical trials of tirasemtiv and omecamtiv mecarbil enroll patients who typically suffer from serious diseases which put them at increased risk of death. These patients may die while receiving our drug candidates. In such circumstances, it may not be possible to exclude with certainty a causal relationship to our drug candidate, even though the responsible clinical investigator may view such an event as not study drug-related.

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 more years. However, the clinical trials for all or any of our 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:

S-6

Table of Contents

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 and other entities involved in the conduct of our clinical trials;

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 oral formulation for omecamtiv mecarbil;

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;

a regulatory authority may require changes to a protocol for a clinical trial that then may require approval from regulatory agencies in other jurisdictions where the trial is being conducted;

an institutional review board (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, or delays in the manufacture or supply, of clinical trial materials;

uncertain dosing issues;

failure by us, our partners, or clinical research organizations, investigators or site personnel engaged by us or our partners to comply with good clinical practices and other applicable laws and regulations, including those concerning informed consent;

inability or unwillingness of investigators or their staffs to follow clinical protocols;

failure by our clinical research organizations, clinical manufacturing organizations and other third parties supporting our clinical trials to fulfill their obligations;

inability to monitor patients adequately during or after treatment;

introduction of new therapies or changes in standards of practice or regulatory guidance that render our drug candidates or their clinical trial endpoints obsolete; and

results from non-clinical studies that may adversely impact the timing or further development of our drug candidates.

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 depend on Amgen for the conduct, completion and funding of the clinical development and commercialization of omecamtiv mecarbil.

Under our strategic alliance, Amgen holds an exclusive license to our drug candidate omecamtiv mecarbil worldwide. As a result, Amgen is responsible for the clinical development and obtaining and maintaining regulatory approval of omecamtiv mecarbil for the potential treatment of heart failure worldwide.

S-7

Table of Contents

We do not control the clinical development activities being conducted or that may be conducted in the future by Amgen, including, but not limited to, 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 Amgen's results. Amgen may conduct these activities more slowly or in a different manner than we would if we controlled the clinical development of omecamtiv mecarbil. Amgen is responsible for filing future applications with the FDA or other regulatory authorities for approval of omecamtiv mecarbil and will be the owner of any marketing approvals issued by the FDA or other regulatory authorities for omecamtiv mecarbil. If the FDA or other regulatory authorities approve omecamtiv mecarbil, Amgen will also be responsible for the marketing and sale of the resulting drug, subject to our right to co-promote omecamtiv mecarbil in North America if we exercise our option to co-fund Phase III development costs of omecamtiv mecarbil under the collaboration. However, we cannot control whether Amgen will devote sufficient attention and resources to the clinical development of omecamtiv mecarbil or will proceed in an expeditious manner, even if we do exercise our option to co-fund the development of omecamtiv mecarbil. Even if the FDA or other regulatory agencies approve omecamtiv mecarbil, Amgen may elect not to proceed with the commercialization of the resulting drug in one or more countries.

If the results of one or more clinical trials with omecamtiv mecarbil do not meet Amgen's expectations at any time, Amgen may elect to terminate further development of omecamtiv mecarbil or certain of the potential clinical trials for omecamtiv mecarbil, even if the actual number of patients treated at that time is relatively small. In addition, Amgen generally has discretion to elect whether to pursue or abandon the development of omecamtiv mecarbil and may terminate our strategic alliance for any reason upon six months prior notice. If Amgen abandons omecamtiv mecarbil, it would result in a delay in or could prevent us from commercializing omecamtiv mecarbil, and would delay and could prevent us from obtaining revenues for this drug candidate. Disputes may arise between us and Amgen, which may delay or cause the termination of any omecamtiv mecarbil clinical trials, result in significant litigation or cause Amgen to act in a manner that is not in our best interest. If development of omecamtiv mecarbil does not progress for these or any other reasons, we would not receive further milestone payments or royalties on product sales from Amgen with respect to omecamtiv mecarbil. If Amgen abandons development of omecamtiv mecarbil prior to regulatory approval or if it elects not to proceed with commercialization of the resulting drug following regulatory approval, we would have to seek a new partner for clinical development or commercialization, curtail or abandon that clinical development or commercialization, or undertake and fund the clinical development of omecamtiv mecarbil or commercialization of the resulting drug ourselves. If we seek a new partner but are unable to do so on acceptable terms, or at all, or do not have sufficient funds to conduct the development or commercialization of omecamtiv mecarbil ourselves, we would have to curtail or abandon that development or commercialization, which could harm our business.

We will depend on Astellas for the conduct, completion and funding of the clinical development and commercialization of CK-2127107.

In June 2013, we entered into a strategic alliance with Astellas focused on the research, development and commercialization of skeletal muscle activators, other than tirasemtiv and certain related compounds. The primary objective of the strategic alliance is to advance novel therapies for indications associated with muscle weakness.

As part of the strategic alliance, we granted Astellas an exclusive license to co-develop and commercialize CK-2127107 for potential application in non-neuromuscular indications worldwide. Following Cytokinetics' conduct of Phase I clinical trials and certain Phase II readiness activities for CK-2127107, Astellas will be primarily responsible for the conduct of subsequent development and commercialization activities for CK-2127107. Astellas may elect not to continue development of CK-2127107 following Cytokinetics' completion of these activities. In such event, we would need significant additional funding to continue the development of CK-2127107 on our own, which may not be available on attractive or acceptable terms, if at all, and we would be limited in the indications that we

could pursue with this drug candidate.

We do not control the clinical development activities that may be conducted by Astellas, including, but not limited to, 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 Astellas' results. Astellas may conduct these activities more slowly or in a different manner than we would. Astellas is responsible for filing future applications with the FDA or other regulatory authorities for approval of CK-2127107 and will be the owner of any marketing approvals issued by the FDA or other regulatory authorities for CK-2127107. If the FDA or other regulatory authorities approve CK-2127107, Astellas will also be responsible for the marketing and sale of the resulting drug, subject to our right to co-promote the drug in the United States and Canada. However, we cannot control whether Astellas will devote sufficient attention and resources to the clinical development of CK-2127107 or will proceed in an expeditious manner. Even if the FDA or other regulatory agencies approve CK-2127107, Astellas may elect not to proceed with the commercialization of the resulting drug in one or more countries.

S-8

Table of Contents

If the results of one or more clinical trials with CK-2127107 do not meet Astellas' expectations at any time, Astellas may elect to terminate further development of CK-2127107 or certain of the potential clinical trials for CK-2127107, even if the actual number of patients treated at that time is relatively small. In addition, Astellas generally has discretion to elect whether to pursue or abandon the development of CK-2127107. Astellas may terminate our strategic alliance in whole or in part for any reason upon six months prior notice at any time following expiration of the strategic alliance's two-year research term. If Astellas abandons CK-2127107, it would result in a delay in or could prevent us from further developing or commercializing CK-2127107, and would delay and could prevent us from obtaining revenues for this drug candidate. Disputes may arise between us and Astellas, which may delay or cause the termination of any CK-2127107 clinical trials, result in significant litigation or cause Astellas to act in a manner that is not in our best interest. If development of CK-2127107 does not progress for these or any other reasons, we would not receive further milestone payments or royalties on product sales from Astellas with respect to CK-2127107. If Astellas abandons development of CK-2127107 prior to regulatory approval or if it elects not to proceed with commercialization of the resulting drug following regulatory approval, we would have to seek a new partner for clinical development or commercialization, curtail or abandon that clinical development or commercialization, or undertake and fund the clinical development of CK-2127107 or commercialization of the resulting drug ourselves. If we seek a new partner but are unable to do so on acceptable terms, or at all, or do not have sufficient funds to conduct the development or commercialization of CK-2127107 ourselves, we would have to curtail or abandon that development or commercialization, which could harm our business.

If we do not enter into strategic alliances for our unpartnered drug candidates or research and development programs or fail to successfully maintain our current or future strategic alliances, we may have to reduce, delay or discontinue our advancement of our drug candidates and programs or expand our research and development capabilities and increase our expenditures.

Drug development is complicated and expensive. We currently have limited financial and operational resources to carry out drug development. Our strategy for developing, manufacturing and commercializing our drug candidates currently requires us to enter into and successfully maintain strategic alliances with pharmaceutical companies or other industry participants to advance our programs and reduce our expenditures on each program. Accordingly, the success of our development activities depends in large part on our current and future strategic partners' performance, over which we have little or no control.

We have retained the rights to develop and commercialize tirasemtiv. We currently do not have a strategic partner for this drug candidate. We may seek one or more strategic partners or other arrangements with third parties to support Phase III clinical development and commercialization of tirasemtiv. However, we may not be able to negotiate and enter into such strategic alliances or arrangements on acceptable terms, if at all, or in accordance with our planned timelines. If we are unable to enter into a strategic alliance for tirasemtiv, we will be unable to conduct the one or more Phase III clinical trials we believe will be necessary to obtain marketing approval for tirasemtiv for the potential treatment of ALS unless we are able to acquire the funding to do so from another source.

Our ability to commercialize drugs that we develop with our partners and that generate royalties from product sales depends on our partners' abilities to assist us in establishing the safety and efficacy of our drug candidates, obtaining and maintaining regulatory approvals and achieving market acceptance of the drugs once commercialized. Our partners may elect to delay or terminate development of one or more drug candidates, independently develop drugs that could compete with ours or fail to commit sufficient resources to the marketing and distribution of drugs developed through their strategic alliances with us. Our partners may not proceed with the development and commercialization of our drug candidates with the same degree of urgency as we would because of other priorities they face. In addition, new business combinations or changes in a partner's business strategy may adversely affect its willingness or ability to carry out its obligations under a strategic alliance.

If we are not able to successfully maintain our existing strategic alliances or establish and successfully 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. Alternatively, if we elect to continue to conduct any of these drug development programs or research programs on our own, we will need to expand our capability to conduct clinical development by bringing additional skills, technical expertise and resources into our organization. This would require significant additional funding, which may not be available to us on acceptable terms, or at all.

To the extent we elect to fund the development of a drug candidate, such as omecamtiv mecarbil, tirasemtiv or CK-2127107, or the commercialization of a drug at our expense, we will need substantial additional funding.

The discovery, development and commercialization of new drugs is costly. As a result, to the extent we elect to fund the development of a drug candidate, such as omecamtiv mecarbil, tirasemtiv or CK-2127107, or the commercialization of a drug, we will need to raise additional capital to:

fund clinical trials and seek regulatory approvals;

expand our development capabilities;

S-9

Table of Contents

engage third party manufacturers for such drug candidate or drug;

build or access commercialization capabilities;

implement additional internal systems and infrastructure;

maintain, defend and expand the scope of our intellectual property; and

hire and support additional management and scientific personnel.

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

the rate of progress and costs of our clinical trials and other research and development activities;

the costs and timing of seeking and obtaining regulatory approvals;

the costs associated with establishing manufacturing and commercialization capabilities;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

the costs of acquiring or investing in businesses, products and technologies;

the effect of competing technological and market developments; and

the status of, payment and other terms, and timing of any strategic alliance, licensing or other arrangements that we have entered into or may establish.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to continue to finance our future cash needs primarily through strategic alliances, public or private equity offerings and debt financings. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are not able to secure additional funding when needed, we may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or future commercialization initiatives.

We depend on contract research organizations to conduct our clinical trials and have limited control over their performance.

We have used and intend to continue to use contract research organizations (CROs) within and outside of the United States to conduct clinical trials of our drug candidates, such as tirasemtiv, CK-2127107 and omecamtiv mecarbil, and related activities. We do not have control over many aspects of our CROs' activities, and cannot fully control the amount, timing or quality of resources that they devote to our programs. CROs may not assign as high a priority to our programs or pursue them as diligently as we would if we were undertaking these programs ourselves. The activities conducted by our CROs therefore may not be completed on schedule or in a satisfactory manner. CROs may also give higher priority to relationships with our competitors and potential competitors than to their relationships with us. Outside of the United States, we are particularly dependent on our CROs' expertise in communicating with clinical trial sites and regulatory authorities and ensuring that our clinical trials and related activities and regulatory filings comply with applicable laws.

Our CROs' failure to carry out development activities on our behalf as agreed and in accordance with our and the FDA's or other regulatory agencies' requirements and applicable U.S. and foreign laws, or our failure to properly coordinate and manage these activities, could increase the cost of our operations and delay or prevent the development, approval and commercialization of our drug candidates. For example, in June 2013 we learned from our data management vendor for our BENEFIT-ALS clinical trial that a programming error in the electronic data capture system controlling study drug assignment caused 58 patients initially randomized to and treated with tirasemtiv to receive placebo instead at a certain trial visit and for the remainder of the trial. In order to maintain the originally intended statistical power of the trial, we amended the protocol to permit enrollment of approximately 680 patients, or 180 patients in addition to the 500 patients allowed under the existing protocol. This protocol amendment will result in additional costs and delays in conducting BENEFIT-ALS. In addition, if a CRO fails to perform as agreed, our ability to collect damages may be contractually limited. If we fail to effectively manage the CROs carrying out the development of our drug candidates or if our CROs fail to perform as agreed, the commercialization of our drug candidates will be delayed or prevented.

We have no manufacturing capacity and depend on our strategic partners and contract manufacturers to produce our clinical trial materials, including our drug candidates, and anticipate continued reliance on contract manufacturers for the development and commercialization of our potential drugs.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates. We have limited experience in drug formulation and manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale. Amgen has assumed responsibility to conduct these activities for the ongoing clinical development of omecamtiv mecarbil worldwide. Following our conduct of the Phase I clinical trials for CK-2127107, Astellas will assume responsibility to conduct these activities for the ongoing clinical development of CK-2127107 worldwide. For tirasemtiv,

Table of Contents

we rely on a limited number of contract manufacturers. In particular, we rely on single-source contract manufacturers for the active pharmaceutical ingredient and the drug product supply for our clinical trials, as well as other materials required to conduct our clinical trials. We expect to rely on contract manufacturers to supply all future drug candidates for which we conduct clinical development, as well as other materials required to conduct our clinical trials. If any of our existing or future contract manufacturers fail to perform satisfactorily, it could delay clinical development or regulatory approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential product revenues. In addition, if a contract manufacturer fails to perform as agreed, our ability to collect damages may be contractually limited.

Our drug candidates require precise high-quality manufacturing. The failure to achieve and maintain high manufacturing standards, including failure to detect or control anticipated or unanticipated manufacturing errors or the frequent occurrence of such errors, could result in patient injury or death, discontinuance or delay of ongoing or planned clinical trials, delays or failures in product testing or delivery, cost overruns, product recalls or withdrawals and other problems that could seriously hurt our business. Contract drug manufacturers often encounter difficulties involving production yields, quality control and quality assurance and shortages of qualified personnel. These manufacturers are subject to stringent regulatory requirements, including the FDA's current good manufacturing practices regulations and similar foreign laws and standards. Each contract manufacturer must pass a pre-approval inspection before we can obtain marketing approval for any of our drug candidates and following approval will be subject to ongoing periodic unannounced inspections by the FDA, the U.S. Drug Enforcement Agency and other regulatory agencies, to ensure strict compliance with current good manufacturing practices and other applicable government regulations and corresponding foreign laws and standards. We seek to ensure that our contract manufacturers comply fully with all applicable regulations, laws and standards. However, we do not have control over our contract manufacturers' compliance with these regulations, laws and standards. If one of our contract manufacturers fails to pass its pre-approval inspection or maintain ongoing compliance at any time, the production of our drug candidates could be interrupted, resulting in delays or discontinuance of our clinical trials, additional costs and potentially lost revenues. In addition, failure of any third party manufacturers or us to comply with applicable regulations, including pre-or post-approval inspections and the current good manufacturing practice requirements of the FDA or other comparable regulatory agencies, could result in sanctions being imposed on us. These sanctions could include fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delay, suspension or withdrawal of approvals, license revocation, product seizures or recalls, operational restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

In addition, our existing and future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our drug candidates. If a natural disaster, business failure, strike or other difficulty occurs, we may be unable to replace these contract manufacturers in a timely or cost-effective manner and the production of our drug candidates would be interrupted, resulting in delays and additional costs.

Switching manufacturers or manufacturing sites would be difficult and time-consuming because the number of potential manufacturers is limited. In addition, before a drug from any replacement manufacturer or manufacturing site can be commercialized, the FDA and, in some cases, foreign regulatory agencies, must approve that site. These approvals would require regulatory testing and compliance inspections. A new manufacturer or manufacturing site also would have to be educated in, or develop substantially equivalent processes for, production of our drugs and drug candidates. It may be difficult or impossible to transfer certain elements of a manufacturing process to a new manufacturer or for us to find a replacement manufacturer on acceptable terms quickly, or at all, either of which would delay or prevent our ability to develop drug candidates and commercialize any resulting drugs.

We may not be able to successfully scale-up manufacturing of our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing resulting approved drugs, if any.

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

S-11

Table of Contents

The mechanisms of action of our drug candidates are unproven, and we do not know whether we will be able to develop any drug of commercial value.

We have discovered and are currently developing drug candidates that have what we believe are novel mechanisms of action directed against cytoskeletal targets, and intend to continue to do so. Because no currently approved drugs appear to operate via the same biochemical mechanisms as our compounds, we cannot be certain that our drug candidates will result in commercially viable drugs that safely and effectively treat the indications for which we intend to develop them. The results we have seen for our compounds in preclinical models may not translate into similar results in humans, and results of early clinical trials in humans may not be predictive of the results of larger clinical trials that may later be conducted with our drug candidates. Even if we are successful in developing and receiving regulatory approval for a drug candidate for the treatment of a particular disease, we cannot be certain that it will be accepted by prescribers or be reimbursed by insurers or that we will also be able to develop and receive regulatory approval for that or other drug candidates for the treatment of other diseases. If we or our partners are unable to successfully develop and commercialize our drug candidates, our business will be materially harmed.

Our success depends substantially upon our ability to obtain and maintain intellectual property protection relating to our drug candidates, compounds and research technologies.

We own, or hold exclusive licenses to, a number of U.S. and foreign patents and patent applications directed to our drug candidates, compounds and research technologies. Our success depends on our ability to obtain patent protection both in the United States and in other countries for our drug candidates, their methods of manufacture and use, and our technologies. Our ability to protect our drug candidates, compounds and technologies from unauthorized or infringing use by third parties depends substantially on our ability to obtain and enforce our patents. If our issued patents and patent applications, if granted, do not adequately describe, enable or otherwise provide coverage of our technologies and drug candidates, including omecamtiv mecarbil, tirasemtiv and CK-2127107, we or our licensees would not be able to exclude others from developing or commercializing these drug candidates. Furthermore, the degree of future protection of our proprietary rights is uncertain because legal means may not adequately protect our rights or permit us to gain or keep our competitive advantage.

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 provide us with any significant protection against competitive products, or will afford us a commercial advantage over competitive products. In particular:

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.

S-12

Table of Contents

Patent protection is afforded on a country-by-country basis. Some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States. Many companies have encountered significant difficulties in protecting and defending intellectual property rights in foreign jurisdictions. Some of our development efforts are performed in countries outside of the United States through third party contractors. We may not be able to effectively monitor and assess intellectual property developed by these contractors. We therefore may not be able to effectively protect this intellectual property and could lose potentially valuable intellectual property rights. In addition, the legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective of intellectual property rights as in the United States. Therefore, we may be unable to acquire and protect intellectual property developed by these contractors to the same extent as if these development activities were being conducted in the United States. If we encounter difficulties in protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed.

We rely on intellectual property assignment agreements with our corporate partners, employees, consultants, scientific advisors and other collaborators to grant us ownership of new intellectual property that is developed. These agreements may not result in the effective assignment to us of that intellectual property. As a result, our ownership of key intellectual property could be compromised.

Changes in either the patent laws or their interpretation in the United States or other countries may diminish the value of our intellectual property or our ability to obtain patents. For example, the America Invents Act of 2011 may affect the scope, strength and enforceability of our patent rights in the United States or the nature of proceedings which may be brought by us related to our patent rights in the United States.

If one or more products resulting from our drug candidates is approved for sale by the FDA and we do not have adequate intellectual property protection for those products, competitors could duplicate them for approval and sale in the United States without repeating the extensive testing required of us or our partners to obtain FDA approval. Regardless of any patent protection, under current law, an application for a generic version of a new chemical entity cannot be approved until at least five years after the FDA has approved the original product. When that period expires, or if that period is altered, the FDA could approve a generic version of our product regardless of our patent protection. An applicant for a generic version of our product may only be required to conduct a relatively inexpensive study to show that its product is bioequivalent to our product, and may not have to repeat the lengthy and expensive clinical trials that we or our partners conducted to demonstrate that the product is safe and effective. In the absence of adequate patent protection for our products in other countries, competitors may similarly be able to obtain regulatory approval in those countries of generic versions of our products.

We also rely on trade secrets to protect our technology, particularly where we believe patent protection is not appropriate or obtainable. However, trade secrets are often difficult to protect, especially outside of the United States. While we endeavor to use reasonable efforts to protect our trade secrets, our or our partners' employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our information to competitors. In addition, confidentiality agreements, if any, executed by those individuals may not be enforceable or provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure. Pursuing a claim that a third party had illegally obtained and was 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, if our competitors independently develop information equivalent or similar to our trade secrets, our business could be harmed.

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

profitability.

If we are sued for infringing third party intellectual property rights, it will be costly and time-consuming, and an unfavorable outcome could have a significant adverse effect on 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. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the therapeutic areas in which we are developing drug candidates and seeking new potential drug candidates. In addition, because patent applications can take several years to issue, there may be currently pending applications, unknown to us, which could later result in issued patents that our activities with our drug candidates could infringe. There may also be existing patents, unknown to us, that our activities with our drug candidates could infringe.

Other future products of ours may be impacted by patents of companies engaged in competitive programs with significantly greater resources. Further development of these products could be impacted by these patents and result in significant legal fees.

S-13

Table of Contents

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

infringement and other intellectual property claims that, even if meritless, can be costly and time-consuming to litigate, delay the regulatory approval process and divert management's attention from our core business operations;

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

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

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

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

We may undertake infringement or other legal proceedings against third parties, causing us to spend substantial resources on litigation and exposing our own intellectual property portfolio to challenge.

Third parties may infringe our patents. To prevent infringement or unauthorized use, we may need to file infringement suits, which are expensive and time-consuming. In an infringement proceeding, a court may decide that one or more of our patents is invalid, unenforceable, or both. In this case, third parties may be able to use our technology without paying licensing fees or royalties. Even if the validity of our patents is upheld, a court may refuse to stop the other party from using the technology at issue on the ground that the other party's activities are not covered by our patents. Policing unauthorized use of our intellectual property is difficult, and we may not be able to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. In addition, third parties may affirmatively challenge our rights to, or the scope or validity of, our patent rights.

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

Inventions discovered under our current or future strategic alliance agreements may become jointly owned by our strategic partners and us in some cases, and the exclusive property of one of us in other cases. Under some circumstances, it may be difficult to determine who owns a particular invention or whether it is jointly owned, and disputes could arise regarding ownership or use of those inventions. These disputes could be costly and time-consuming, and an unfavorable outcome could have a significant adverse effect on our business if we were not able to protect or license rights to these inventions. In addition, our research collaborators and clinical investigators generally have contractual rights to publish data arising from their work. Publications by our research collaborators and clinical investigators relating to our research and development programs, either with or without our consent, could benefit our current or potential competitors and may impair our ability to obtain patent protection or protect our proprietary information, which could significantly harm our business.

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

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

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.

We compete with companies that have developed drugs or are developing drug candidates for cardiovascular diseases, diseases and conditions associated with muscle weakness or wasting and other diseases for which our drug candidates may be useful treatments. For example, if tirasemtiv is approved for marketing by the FDA or other regulatory authorities for the treatment of ALS, it may then compete with other potential new therapies for ALS that are currently being developed by companies such as Mitsubishi

Table of Contents

Tanabe Pharma Corporation, Eisai Inc., Trophos SA, Neuraltus Pharmaceuticals, Inc., Isis Pharmaceuticals, Inc. and GlaxoSmithKline plc. In addition, BrainStorm Cell Therapeutics and Neuralstem, Inc. are each conducting clinical development of stem cell therapies for the potential treatment of ALS. If CK-2127107 is approved by the FDA for the potential treatment of non-neuromuscular indications associated with muscle weakness, potential competitors include Ligand Pharmaceuticals, Inc., which is developing LGD-4033, a selective androgen receptor modulator, for muscle wasting; and GTx, Inc., which is developing ostarine, a selective androgen receptor modulator, for cancer cachexia and potentially other indications. Novartis (in collaboration with Morphosys AG), is conducting clinical development with an activin type-IIIB receptor antagonist, bimagrumab, to evaluate its ability to treat diseases involving the loss of muscle mass, strength and function. Drugs that could compete with CK-2127107 could also compete against tirasemtiv in ALS or other neuromuscular diseases, should the appropriate clinical trials be conducted.

If omecamtiv mecarbil is approved for marketing by the FDA or other regulatory authorities for heart failure, it would compete against other drugs used for the treatment of acute and chronic heart failure. These include generic drugs, such as milrinone, dobutamine or digoxin and branded drugs such as Natrecor (nesiritide). Omecamtiv mecarbil could also potentially compete against other novel drug candidates and therapies in development, such as bucindolol, which is being developed by ARCA biopharma, Inc.; sererelaxin and LCZ-696, which are being developed by Novartis; cenderitide (CD-NP), which is being developed by Carpicor Therapeutics, Inc., TRV-027, which is being developed by Trevena; ularitide, which is being developed by Cardiorientis Ltd.; aladorian, which is being developed by Armgo Pharma, Inc; certain cardioprotectants which are being developed by Cardioxyl Pharmaceuticals, Inc.; glial growth factor (GGF-2) which is being developed by Acorda Therapeutics, Inc.; Neurocardin, which is being developed by Zensun Sci & Tech, Ltd; Mydicar, a genetically-targeted enzyme replacement therapy for advanced heart failure which is being developed by Celladon Corporation; and levosimendan, which was recently acquired for development by Oxygen Biotherapeutics, Inc. In addition, there are a number of medical devices being developed for the potential treatment of heart failure.

Our competitors may:

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

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

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

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

more successfully recruit skilled scientific workers and management from the limited pool of available talent;

more effectively negotiate third-party licenses and strategic alliances;

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

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

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

developing drug candidates;

undertaking preclinical testing and clinical trials;

building relationships with key customers and opinion-leading physicians;

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

formulating and manufacturing drugs; and

launching, marketing and selling drugs.

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

Table of Contents

Our failure to attract and retain skilled personnel could impair our drug development and commercialization activities.

Our business depends on the performance of our senior management and key scientific and technical personnel. The loss of the services of any member of our senior management or key scientific or technical staff may significantly delay or prevent the achievement of drug development and other business objectives by diverting management's attention to transition matters and identifying suitable replacements. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us. In addition, if and as our business grows, we will need to recruit additional executive management and scientific and technical personnel. There is intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. Our inability to attract and retain sufficient scientific, technical and managerial personnel could limit or delay our product development activities, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

Any future workforce and expense reductions may have an adverse impact on our internal programs and our ability to hire and retain skilled personnel.

Our future success will depend in large part upon our ability to attract and retain highly skilled personnel. In light of our continued need for funding and cost control, we may be required to implement future workforce and expense reductions, which could further limit our research and development activities. For example, in October 2011, we reduced our workforce by approximately 18% in order to reduce expenses and to focus resources primarily on our later-stage development programs for tirasemtiv and omecamtiv mecarbil and certain other research and development programs also directed to muscle biology. Any headcount reductions or other cost control measures we may implement could negatively affect our productivity and limit our research and development activities. We may have difficulty retaining and attracting such personnel as a result of a perceived risk of future workforce reductions. In addition, the implementation of any additional workforce or expense reduction programs may divert the efforts of our management team and other key employees, which could adversely affect our business.

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

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

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

We currently have no sales, marketing or distribution capabilities. We plan to commercialize drugs that can be effectively marketed and sold in concentrated markets that do not require a large sales force to be competitive. To

achieve this goal, we will need to establish our own specialized sales force and marketing organization with technical expertise and supporting distribution capabilities. Developing such an organization is expensive and time-consuming and could delay a product launch. In addition, we may not be able to develop this capacity efficiently, cost-effectively or at all, which could make us unable to commercialize our drugs. If we determine not to market our drugs on our own, we will depend on strategic alliances with third parties, such as Amgen and Astellas, which have established distribution systems and direct sales forces to commercialize them. If we are unable to enter into such arrangements on acceptable terms, we may not be able to successfully commercialize these drugs. To the extent that we are not successful in commercializing any drugs ourselves or through a strategic alliance, our product revenues and business will suffer and our stock price would decrease.

S-16

Table of Contents

Risks Related To Our Industry

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

The research, testing, manufacturing, selling and marketing of drugs are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, and regulations differ from country to country. Neither we nor our partners are permitted to market our potential drugs in the United States until we receive approval of a new drug application (NDA) from the FDA. Neither we nor our partners have received NDA or other marketing approval for any of Cytokinetics' drug candidates.

Obtaining NDA approval is a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable foreign and U.S. regulatory requirements may subject us to administrative or judicially imposed sanctions. These include warning letters, civil and criminal penalties, injunctions, product seizure or detention, product recalls, total or partial suspension of production, and refusal to approve pending NDAs or supplements to approved NDAs.

Regulatory approval of an NDA or NDA supplement is never guaranteed, and the approval process typically takes several years and is extremely expensive. The FDA and foreign regulatory agencies also have substantial discretion in the drug approval process, and the guidance and advice issued by such agencies is subject to change at any time. Despite the time and efforts exerted, failure can occur at any stage, and we may encounter problems that cause us to abandon clinical trials or to repeat or perform additional preclinical testing and clinical trials. The number and focus of preclinical studies and clinical trials that will be required for approval by the FDA and foreign regulatory agencies varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. In addition, the FDA may require that a proposed Risk Evaluation and Mitigation Strategy, also known as a REMS, be submitted as part of an NDA if the FDA determines that it is necessary to ensure that the benefits of the drug outweigh its risks. The FDA and foreign regulatory agencies can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to:

they might determine that a drug candidate is not safe or effective;

they might not find the data from preclinical testing and clinical trials sufficient and could request that additional trials be performed;

they might not approve our, our partner's or the contract manufacturer's processes or facilities; or

they might change their approval policies or adopt new regulations.

Even if we receive regulatory approval to manufacture and sell a drug in a particular regulatory jurisdiction, other jurisdictions' regulatory authorities may not approve that drug for manufacture and sale. If we or our partners fail to receive and maintain regulatory approval for the sale of any drugs resulting from our drug candidates, it would significantly harm our business and negatively affect our stock price.

If we or our partners receive regulatory approval for our drug candidates, we or they will be subject to ongoing obligations to and continued regulatory review by the FDA and foreign regulatory agencies, and may be subject to additional post-marketing obligations, all of which may result in significant expense and limit commercialization of our potential drugs.

Any regulatory approvals that we or our partners receive for our drug candidates may be subject to limitations on the indicated uses for which the drug may be marketed or require potentially costly post-marketing follow-up studies or compliance with a REMS. In addition, if the FDA or foreign regulatory agencies approves any of our drug candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including adverse events of unanticipated severity or frequency, or the discovery that adverse effects or toxicities observed in preclinical research or clinical trials that were believed to be minor actually constitute much more serious problems, may result in restrictions on the marketing of the drug or withdrawal of the drug from the market.

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

S-17

Table of Contents

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

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

introduction of competitive drugs to the market;

clinical safety and efficacy of alternative drugs or treatments;

cost-effectiveness;

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

convenience and ease of administration;

prevalence and severity of adverse side effects;

other potential disadvantages relative to alternative treatment methods; or

insufficient marketing and distribution support.

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

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

Even if one or more of our drug candidates is approved for sale, the commercial success of our drugs in both domestic and international markets will be substantially dependent on whether third-party coverage and reimbursement is available for our drugs by the medical profession for use by their patients, which is highly uncertain. Medicare, Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. As a result, they may not cover or provide adequate payment for our drugs. They may not view our drugs as cost-effective and reimbursement may not be available to consumers or may be insufficient to allow our drugs to be marketed on a competitive basis. If we are unable to obtain adequate coverage and reimbursement for our drugs, our ability to generate revenue will be adversely affected. Likewise, current and future legislative or regulatory efforts to control or reduce healthcare costs

or reform government healthcare programs, such as the Patient Protection Affordable Care Act and the Health Care and Education Reconciliation Act of 2010, could result in lower prices or rejection of coverage and reimbursement for our potential drugs. Changes in coverage and reimbursement policies or healthcare cost containment initiatives that limit or restrict reimbursement for any of our drug candidates that are approved could cause our potential future revenues to decline.

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

The use of our drug candidates in clinical trials may result in adverse effects. We cannot predict all the possible harms or adverse effects that may result from our clinical trials. We currently maintain limited product liability insurance. We may not have sufficient resources to pay for any liabilities resulting from a personal injury or other claim excluded from, or beyond the limit of, our insurance coverage. Our insurance does not cover third parties' negligence or malpractice, and our clinical investigators and sites may have inadequate insurance or none at all. In addition, in order to conduct clinical trials or otherwise carry out our business, we may have to contractually assume liabilities for which we may not be insured. If we are unable to look to our own or a third party's insurance to pay claims against us, we may have to pay any arising costs and damages ourselves, which may be substantial.

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

Table of Contents

We may be required to indemnify third parties against damages and other liabilities arising out of our development, commercialization and other business activities, which could be costly and time-consuming and distract management. If third parties that have agreed to indemnify us against damages and other liabilities arising from their activities do not fulfill their obligations, then we may be held responsible for those damages and other liabilities.

Our employees or contractors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, anti-fraud and abuse laws, anti-bribery laws and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees or contractors. Such misconduct could include failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with anti-bribery laws (such as the Foreign Corrupt Practice Act) or healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, marketing and promotion, sales commission, incentive programs and other business arrangements and practices. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent these activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Responding to any claims relating to improper handling, storage or disposal of the hazardous chemicals and radioactive and biological materials we use in our business could be time-consuming and costly.

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

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

All of our facilities and our important documents and records, such as hard copies of our laboratory books and records for our drug candidates and compounds and our electronic business records, are located in our corporate headquarters at a single location in South San Francisco, California near active earthquake zones. If a natural disaster, such as an earthquake or flood, a catastrophic event such as a disease pandemic or terrorist attack, or a localized extended outage of critical utilities or transportation systems occurs, we could experience a significant business interruption. Our partners and other third parties on which we rely may also be subject to business interruptions from such events. In addition, California from time to time has experienced shortages of water, electric power and natural gas. Future shortages and conservation measures could disrupt our operations and cause expense, thus adversely affecting our business and financial results.

Risks Related To an Investment in Our Securities

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

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

announcements concerning any of the clinical trials for our drug candidates, such as tirasemtiv for the potential treatment of ALS, CK-2127107 for the potential treatment of non-neuromuscular indications associated with muscle weakness and omecamtiv mecarbil for the potential treatment of heart failure (including, but not limited to, the timing of initiation or completion of such trials and the results of such trials, and delays or discontinuations of such trials, including delays resulting from slower than expected or suspended patient enrollment or discontinuations resulting from a failure to meet pre-defined clinical end points);

S-19

Table of Contents

announcements concerning our strategic alliance with Amgen or Astellas or future strategic alliances;

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

failure or discontinuation of any of our research programs;

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

failure or delay in establishing new strategic alliances, or the terms of those alliances;

market conditions in the pharmaceutical, biotechnology and other healthcare-related sectors;

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

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

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

issues in manufacturing our drug candidates or drugs;

market acceptance of our drugs;

third-party healthcare coverage and reimbursement policies;

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

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

additions or departures of key personnel;

substantial sales of our common stock by our existing stockholders, whether or not related to our performance;

automated trading activity by algorithmic and high-frequency trading programs; and

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

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

As of January 31, 2014, our executive officers, directors and their affiliates beneficially owned or controlled approximately 4.8% of the outstanding shares of our common stock (after giving effect to the exercise of all outstanding vested and unvested options, restricted stock units and warrants). Accordingly, these executive officers, directors and their affiliates, acting as a group, will have substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of us, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

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

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

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

Table of Contents

Our stockholders will experience substantial additional dilution if outstanding options or warrants are exercised for common stock.

As of September 30, 2013, there were 7,692,096 shares of common stock issuable upon the exercise of warrants, having a weighted average exercise price of \$5.95 per share, and 2,451,522 shares of common stock issuable upon the exercise of stock options outstanding, having a weighted average exercise price of \$15.18 per share. The exercise of outstanding options or warrants for common stock would be substantially dilutive to the outstanding shares of common stock. Any dilution or potential dilution may cause our stockholders to sell their shares, which would contribute to a downward movement in the stock price of our common stock.

Ownership changes may limit our ability to use our net operating losses and tax credits in the future.

In general, under Section 382 of the Internal Revenue Code (Section 382), a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change net operating losses and tax credits to offset future taxable income. We have performed a Section 382 analysis and do not believe that we have experienced an ownership change since 2006. A portion of our existing net operating losses and tax credits are subject to limitations arising from previous ownership changes. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 and result in additional limitations. We intend to continue to monitor public filings made by third parties with the SEC to assess whether an ownership change under Section 382 has occurred. Our ability to accurately assess any such ownership change is limited by the timeliness and accuracy of these public filings.

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

Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and new SEC regulations and NASDAQ Stock Market LLC rules create uncertainty for public companies. We regularly evaluate and monitor developments with respect to new and proposed laws, regulations and standards. We cannot accurately predict or estimate the amount of the additional costs we may incur in connection with complying with such laws, regulations and standards or the timing of these costs. For example, compliance with the internal control requirements of Section 404 of the Sarbanes-Oxley Act has to date required us to commit significant resources to document and test the adequacy of our internal control over financial reporting. We can provide no assurance as to conclusions of management or by our independent registered public accounting firm with respect to the effectiveness of our internal control over financial reporting in the future. In addition, the SEC has adopted regulations that require us to file corporate financial statement information in an interactive data format known as XBRL. We may incur significant costs and need to invest considerable resources to remain in compliance with these regulations.

These new or changed laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to maintain high standards of corporate governance and public disclosure. As a result, we intend to invest the resources necessary to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, due to ambiguities related to practice or otherwise, regulatory authorities may initiate legal proceedings against us, which could be costly and time-consuming, and our

reputation and business may be harmed.

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

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

Risks Related to This Offering

If you purchase the common stock sold in this offering, you will experience immediate and substantial dilution in your investment. Raising additional capital by issuing securities in the future will cause dilution to existing stockholders and may cause our share price to decline.

S-21

Table of Contents

Since the price per share of our common stock being offered in this offering is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution with respect to the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$ per share and our net tangible book value as of September 30, 2013, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share with respect to the net tangible book value of the common stock. See the section titled **Dilution** below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

If we issue additional common stock, or securities convertible into or exchangeable or exercisable for common stock following the expiration or earlier waiver of the lock-up agreement we entered into with the underwriters as described in the section titled **Underwriting**, our stockholders, including investors who purchase shares of common stock in this offering, will experience additional dilution, and any such issuances may result in downward pressure on the price of our common stock.

Sales of our common stock through this or other equity offerings could trigger a limitation on our ability to use our net operating losses and tax credits in the future.

The Tax Reform Act of 1986 limits the annual use of net operating loss and tax credit carryforwards in certain situations where changes occur in stock ownership of a company. In the event we have a change in ownership, as defined, the annual utilization of such carryforwards could be limited. This or other equity issuances could trigger a limitation on our ability to use our net operating losses and tax credits in the future under Sections 382 and 383 of the Internal Revenue Code as enacted by the Tax Reform Act of 1986.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock that we are offering will be approximately \$ million, or approximately \$ million if the underwriters exercise in full their option to purchase up to additional shares of common stock, after deducting the underwriting discount and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for research and development and other general corporate purposes, including working capital. We may also use a portion of the net proceeds to acquire or invest in complementary businesses, products and technologies. Although we currently have no material agreements or commitments with respect to acquisitions, we evaluate acquisition opportunities and engage in related discussions from time to time.

Pending application of the net proceeds as described above, we intend to invest the net proceeds in a variety of capital preservation instruments, including direct or guaranteed obligations of the U.S. government, certificates of deposit and money market funds, in accordance with our investment policy.

DIVIDEND POLICY

To date, we have paid no cash dividends to our stockholders, and we do not intend to pay cash dividends in the foreseeable future.

Table of Contents**DILUTION**

Our net tangible book value as of September 30, 2013 was approximately \$39.8 million, or \$1.28 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2013. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this public offering and the net tangible book value per share of our common stock immediately after this public offering.

After giving effect to the sale of _____ shares of our common stock in this offering at the public offering price of \$ _____ per share and after deducting the underwriting discount and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2013 would have been approximately \$ _____, or \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$
Net tangible book value per share of as September 30, 2013	\$ 1.28
Increase in net tangible book value per share attributable to investors purchasing our common stock in this offering	

As adjusted net tangible book value per share after this offering

Dilution per share to investors purchasing our common stock in this offering	\$
--	----

If the underwriters exercise in full their option to purchase up to _____ additional shares of common stock, the as adjusted net tangible book value after this offering would be \$ _____ per share, representing an increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price.

The above discussion and table are based on 29,503,123 shares outstanding as of September 30, 2013, and excludes as of that date:

7,692,096 shares of common stock issuable upon the exercise of _____s outstanding, having a weighted average exercise price of \$5.95 per share;

2,451,522 shares of common stock issuable upon the exercise of stock options outstanding, having a weighted average exercise price of \$15.18 per share;

41,663 units of restricted stock outstanding; and

An aggregate of 2,357,486 shares of common stock reserved for future issuance under our stock option and employee stock purchase plans.

In addition, the number of shares of our common stock to be outstanding immediately after this offering as shown above excludes 1,534,686 shares of common stock that were sold subsequent to September 30, 2013 pursuant to an At-the-Market Issuance Sales Agreement that we entered into with McNicoll, Lewis & Vlak LLC on June 10, 2011.

To the extent that outstanding options or warrants outstanding as of September 30, 2013 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

S-24

Table of Contents**UNDERWRITING**

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock set forth opposite its name below. Cowen and Company, LLC is the representative of the underwriters.

Underwriter	Number of Shares
Cowen and Company, LLC	
JMP Securities LLC	
Total	

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the overallotment option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Overallotment option to purchase additional shares

We have granted to the underwriters an option to purchase up to additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days beginning from the date of this prospectus supplement. The underwriters may exercise this option solely for the purpose of covering overallotments, if any, made in connection with the sale of common stock offered hereby. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and commissions

The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Total
Per Share	

		Without Overallotment	With Overallotment
Public offering price	\$	\$	\$
Underwriting discount			
Proceeds, before expenses, to us			

We estimate that the total expenses of the offering, excluding the underwriting discount, will be approximately \$, which amount includes up to \$100,000 that we have agreed to reimburse the underwriters for their fees and expenses, and such expenses are payable by us.

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of \$ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

S-25

Table of Contents

Discretionary accounts

The underwriters do not intend to confirm sales of the shares to any accounts over which they have discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.

Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriters may close out any short position by exercising their overallotment option and/or purchasing shares in the open market.

Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the overallotment option. If the underwriters sell more shares than could be covered by exercise of the overallotment option and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.

Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on The NASDAQ Capital Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Lock-up agreements

Pursuant to certain lock-up agreements, we and our executive officers and directors, have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic consequence of ownership of, directly or indirectly, or make any demand or request or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, any common stock or securities convertible into or exchangeable or exercisable for any common stock without the prior written consent of Cowen and Company, LLC, for a period of 90 days after the date of the pricing of the offering. The 90-day restricted period will be automatically extended if (i) during the last 17 days of the 90-day restricted period we issue an earnings release or material news or a material event relating to us occurs or (ii) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period, in either of which case the restrictions described above will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the public announcement of the material news or the occurrence of the material event, as applicable, unless Cowen and Company, LLC waives, in writing, such extension.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. The exceptions to the lock-up for executive officers and directors are: (a) transactions relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering; (b) the transfer of shares of common stock or any securities convertible into or exercisable or exchangeable for common stock (i) as a bona fide gift to an immediate family member of the executive officer or director or to a trust formed for the benefit of an immediate family member, (ii) by will or intestate

Table of Contents

succession or (iii) by bona fide gift to a charity or educational institution; (c) the transfer of shares of common stock or any securities convertible into shares of common stock to us to cover tax withholding obligations; and (d) the establishment of a written trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock. The exceptions to the lock-up for us are: (a) the sale of shares of common stock in the offering; (b) the issuance of common stock, options to acquire common stock or other equity awards pursuant to our equity incentive plans and employee stock purchase plan and such other plans and arrangements as are in existence on the date of the underwriting agreement and described in this prospectus supplement or the accompanying prospectus; (c) the issuance of common stock pursuant to the valid exercises, vesting or settlement of options, other equity awards, warrants or rights outstanding on the date of the underwriting agreement; and (d) the issuance of shares of common stock or securities convertible into or exercisable or exchangeable for shares of common stock pursuant to a strategic partnership, joint venture, merger, collaboration, lending or other contractual arrangement, or in connection with the acquisition or license by us of any business, products or technologies, provided, however, that such shares described in this clause (d) may not be traded by the recipient during the 90-day restricted period.

United Kingdom

Each of the underwriters has represented and agreed that:

it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended), or the FSMA, except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority, or FSA;

it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and

it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

Switzerland

The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area

In relation to each Member State of the European Economic Area (Iceland, Norway and Lichtenstein in addition to the member states of the European Union) that has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the

Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, it has not made and will not make an offer of the securities to the public in that Relevant Member State prior to the publication of a prospectus in relation to the securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of the securities to the public in that Relevant Member State at any time:

to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;

in any other circumstances which do not require the publication by the issuer of a prospectus pursuant to Article 3 of the Prospectus Directive.

S-27

Table of Contents

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any securities under, the offer contemplated in this prospectus will be deemed to have represented, warranted and agreed to and with us and each underwriter that:

it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and

in the case of any securities acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (1) the securities acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the representative of the underwriters has been given to the offer or resale; or (2) where securities have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those securities to it is not treated under the Prospectus Directive as having been made to such persons.

For the purposes of the provisions in the two immediately preceding paragraphs, the expression an offer of the securities to the public in relation to the securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Electronic offer, sale and distribution of shares

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representative may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus supplement, the accompanying prospectus or the registration statement of which the accompanying prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other relationships

Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

Table of Contents

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP, Palo Alto, California. Goodwin Procter LLP, New York, New York, is counsel for the underwriters in connection with this offering.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report (which includes an explanatory paragraph relating that the Company is in the development stage and is dependent on its ability to raise additional capital) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the prospectus supplement and before the sale of all the securities covered by this prospectus supplement:

our annual report on Form 10-K for the fiscal year ended December 31, 2012;

the information specifically incorporated by reference into our 2012 Annual Report on Form 10-K referred to above from our definitive proxy statement on Schedule 14A, filed on April 2, 2013;

our quarterly reports on Form 10-Q for the fiscal quarters ended March 31, 2013, June 30, 2013 and September 30, 2013;

our current reports on Form 8-K dated January 25, 2013, February 8, 2013, February 12, 2013, March 11, 2013, March 18, 2013, March 21, 2013, April 1, 2013, May 24, 2013, June 4, 2013, June 12, 2013, June 18, 2013, June 25, 2013, June 25, 2013, July 8, 2013, July 23, 2013, August 22, 2013, September 23, 2013, December 3, 2013, December 10, 2013, December 10, 2013, January 1, 2014, January 13, 2014 and February 19, 2014;

our current reports on Form 8-K dated February 5, 2013, April 30, 2013, July 31, 2013, October 30, 2013 and February 6, 2014 (in each case, as to information therein explicitly filed with the SEC only); and

the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on March 12, 2004, and any further amendment or report filed hereafter for the purpose of updating any such description.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Cytokinetics, Incorporated

280 East Grand Avenue

South San Francisco, California 94080

Edgar Filing: CYTOKINETICS INC - Form 424B5

United States of America

Attn: Investor Relations

(650) 624-3000

S-30

Table of Contents

PROSPECTUS

\$150,000,000

Cytokinetics, Incorporated

COMMON STOCK

PREFERRED STOCK

WARRANTS

From time to time, we may sell any of the securities listed above. All of the securities listed above may be sold individually or in combination with other securities. We may also offer common stock upon conversion of preferred stock, or common stock or preferred stock upon the exercise of warrants. We will specify in an accompanying prospectus supplement the terms of any offering. Our common stock is traded on the NASDAQ Capital Market under the trading symbol CYTK. On November 5, 2013 the last reported sale price of our common stock on the NASDAQ Capital Market was \$6.38 per share. This prospectus describes some of the general terms that may apply to an offering of our securities. The specific terms and any other information relating to a specific offering will be set forth in a post-effective amendment to the registration statement of which this prospectus is a part or in a supplement to this prospectus or may be set forth in one or more documents incorporated by reference in this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with a specific offering.

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

Investing in our securities involves a high degree of risk. See Risk Factors beginning on page 5 of this prospectus. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus, before you make an investment decision.

The securities offered by this prospectus may be offered in amounts, at prices and at terms determined at the time of the offering and may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. We will set forth the names of any underwriters or agents in the accompanying prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution." The net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement. Pursuant to General Instruction I.B.6 of Form S-3, we will not sell our securities in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period if our public float, measured in accordance with such instruction, is below \$75.0 million. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is December 23, 2013

Table of Contents**TABLE OF CONTENTS**

	Page
<u>Prospectus Summary</u>	2
<u>Risk Factors</u>	5
<u>Disclosure Regarding Forward-Looking Statements</u>	5
<u>Use of Proceeds</u>	7
<u>Ratio of Earnings to Combined Fixed Charges and Preference Security Dividends</u>	8
<u>Description of Capital Stock</u>	8
<u>Description of the Warrants</u>	10
<u>Plan of Distribution</u>	13
<u>Legal Matters</u>	14
<u>Experts</u>	14
<u>Where You Can Find More Information</u>	14
<u>Information Incorporated by Reference</u>	14

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

Table of Contents

PROSPECTUS SUMMARY

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

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus, in one or more offerings, up to an aggregate offering price of \$150,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell any securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of those securities. We may also issue a free writing prospectus and/or add, update or change in a prospectus supplement any of the information contained in this prospectus or in documents we have incorporated by reference into this prospectus. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement and any applicable free writing prospectus may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement, including the risk factors, together with any applicable free writing prospectus and the additional information described under the headings Where You Can Find Information and Information Incorporated by Reference.

Cytokinetics, Incorporated

Cytokinetics, Incorporated is 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 most advanced research and development programs relate to the biology of muscle function and are directed to small molecule modulators of the contractility of skeletal or cardiac muscle. We are also conducting or may conduct earlier-stage research directed to other compounds with the potential to modulate muscle contractility and other muscle functions, such as growth, energetics and metabolism.

Our drug candidates currently in clinical development are our skeletal muscle activators, tirasemtiv and CK-2127107, and our cardiac muscle activator, omecamtiv mecarbil. Tirasemtiv is being evaluated for the potential treatment of amyotrophic lateral sclerosis (also known as ALS or Lou Gehrig's disease) and other neuromuscular disorders. CK-2127107 is being evaluated for the potential treatment of non-neuromuscular indications associated with skeletal muscle weakness. Omecamtiv mecarbil is being evaluated for the potential treatment of heart failure.

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

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

Risks Associated with our Business

Our business is subject to numerous risks, as described under the heading **Risk Factors** contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus. These risks include the following, among others:

our ability to acquire the funding necessary to conduct the one or more confirmatory Phase III clinical trials for tirasemtiv in patients with amyotrophic lateral sclerosis that we expect will be required to obtain marketing approval for tirasemtiv for the treatment of ALS;

decisions by Amgen Inc. (**Amgen**) with respect to the timing, design and conduct of research and development activities for omecamtiv mecarbil and other related molecules, including decisions to postpone or discontinue research or development activities relating to omecamtiv mecarbil and other related molecules;

decisions by Astellas Pharma Inc. (**Astellas**) with respect to the timing, design and conduct of research and development activities for CK-2127107 and other skeletal muscle activators, including decisions to postpone or discontinue research or development activities relating to CK-2127107 and other skeletal muscle activators;

Table of Contents

our ability to enter into strategic partnership agreements for any of our programs on acceptable terms and conditions or in accordance with our planned timelines;

our ability to obtain additional financing on acceptable terms, if at all;

our receipt of funds and access to other resources under our current or future strategic alliances or sponsored research arrangements;

difficulties or delays in the development, testing, production or commercialization of our drug candidates;

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

difficulties or delays in the manufacture and supply of clinical trial materials;

failure by our contract research organizations, contract manufacturing organizations and other vendors to properly fulfill their obligations or otherwise perform as expected;

results from non-clinical studies that may adversely impact the timing or the further development of our drug candidates and other compounds;

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;

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;

difficulties or delays in achieving market access and reimbursement for our drug candidates and the potential impacts of health care reform;

changes in laws and regulations applicable to drug development, commercialization or reimbursement;

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

potential infringement or misuse by us of the intellectual property rights of third parties;

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

our ability to issue and sell shares of our common stock under our At-The-Market Issuance Sales Agreement with McNicoll, Lewis & Vlak LLC;

potential ownership changes under Internal Revenue Code Section 382; and

the timeliness and accuracy of information filed with the SEC by third parties.

Table of Contents

The Securities We May Offer

We may offer shares of our common stock and preferred stock, and/or warrants to purchase any of such securities, either individually or in combination with other securities, with a total value of up to \$150,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

designation or classification;

aggregate offering price;

rates and times of payment of interest or dividends, if any;

redemption, conversion, exercise, exchange or sinking fund terms, if any;

voting or other rights, if any;

conversion or exchange prices, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices and in the securities or other property receivable upon conversion or exchange; and

a discussion of material U.S. federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. In this prospectus, we have summarized certain general features of the common stock under *Description of Capital Stock Common Stock*. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors has the authority to designate up to 10,000,000 shares of preferred stock in one or more series and to fix the privileges, preferences and rights of each series of preferred stock, any or all of which may be greater than the rights of the common stock. Our board of directors previously designated 8,070 of the authorized shares of preferred stock as Series A convertible preferred stock, and 23,026 of the authorized shares of preferred stock as Series B convertible preferred stock, none of

Table of Contents

which are currently outstanding. If we sell any new series of preferred stock under this prospectus and any applicable prospectus supplement, our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock being offered, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under "Description of Capital Stock—Preferred Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Warrants. We may issue warrants for the purchase of common stock and/or preferred stock in one or more series. We may issue warrants independently or in combination with common stock and/or preferred stock. In this prospectus, we have summarized certain general features of the warrants under "Description of Warrants." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the warrants. We have filed the forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that we may offer as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Warrants may be issued under a warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if any, in the applicable prospectus supplement relating to a particular series of warrants.

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from this offering, if any, for research and development, general corporate purposes and working capital requirements. See "Use of Proceeds" on page 7 of this prospectus.

NASDAQ Capital Market Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol "CYTK."

RISK FACTORS

An investment in our securities involves a high degree of risk. Before you make a decision to invest in our securities, you should carefully consider the risks described in the section entitled "Risk Factors" contained in our annual report on Form 10-K for the period ended December 31, 2012, as filed with the SEC on March 15, 2013, and our quarterly

reports on Form 10-Q for the periods ended March 31, 2013, June 30, 2013 and September 30, 2013, as filed with the SEC on May 8, 2013, August 7, 2013 and November 6, 2013, respectively, which are incorporated herein by reference in their entirety, as well as any amendment or update thereto reflected in our subsequent filings with the SEC. If any of these risks actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock, or, if applicable, other securities, to decline and you may lose part or all of your investment. The risks described are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business, operating results, prospects or financial condition. The risks discussed below also include forward-looking statements and our actual results may differ substantially from those discussed in these forward-looking statements.

DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

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

Table of Contents

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 2013;

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 anticipated timing of revenue recognition events;

the initiation, design, conduct, enrollment, progress, timing and scope of clinical trials and development activities for our drug candidates conducted by ourselves or our partners, Amgen and Astellas, including the anticipated timing for initiation of clinical trials, anticipated rates of enrollment for clinical trials and anticipated dates of results becoming available or being announced from clinical trials;

the results from the clinical trials and non-clinical and preclinical studies of our drug candidates and other compounds, and the significance and utility of such results;

the ability of our amendment to the protocol of our BENEFIT-ALS clinical trial to maintain the originally intended statistical power of the trial;

our and our partners' plans or ability to conduct the continued research and development of our drug candidates and other compounds;

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

the properties and potential benefits of, and the potential market opportunities for, our drug candidates and other compounds, including the potential indications for which they may be developed;

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

our receipt of milestone payments, royalties, reimbursements and other funds from current or future partners under strategic alliances and sponsored research arrangements, such as with Amgen or Astellas;

our ability to continue to identify additional potential drug candidates that may be suitable for clinical development;

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

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

the utility of our focus on the biology of muscle function, and our ability to leverage our experience in muscle contractility to other muscle functions;

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 loan and lease obligations;

the expected recognition of revenue under our collaboration agreements;

potential competitors and competitive products;

retaining key personnel and recruiting additional key personnel;

expected future amortization of employee stock-based compensation; and

the potential impact of recent accounting pronouncements on our financial position or results of operations. Such forward-looking statements involve risks and uncertainties, including, but not limited to:

our ability to acquire the funding necessary to conduct the one or more confirmatory Phase III clinical trials for tirasemtiv in patients with amyotrophic lateral sclerosis that we expect will be required to obtain

marketing approval for tirasemtiv for the treatment of ALS;

decisions by Amgen with respect to the timing, design and conduct of research and development activities for omecamtiv mecarbil and other related molecules, including decisions to postpone or discontinue research or development activities relating to omecamtiv mecarbil and other related molecules;

decisions by Astellas with respect to the timing, design and conduct of research and development activities for CK-2127107 and other skeletal muscle activators, including decisions to postpone or discontinue research or development activities relating to CK-2127107 and other skeletal muscle activators;

our ability to enter into strategic partnership agreements for any of our programs on acceptable terms and conditions or in accordance with our planned timelines;

Table of Contents

our ability to obtain additional financing on acceptable terms, if at all;

our receipt of funds and access to other resources under our current or future strategic alliances or sponsored research arrangements;

difficulties or delays in the development, testing, production or commercialization of our drug candidates;

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

difficulties or delays in the manufacture and supply of clinical trial materials;

failure by our contract research organizations, contract manufacturing organizations and other vendors to properly fulfill their obligations or otherwise perform as expected;

results from non-clinical studies that may adversely impact the timing or the further development of our drug candidates and other compounds;

the possibility that the 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;

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;

difficulties or delays in achieving market access and reimbursement for our drug candidates and the potential impacts of health care reform;

changes in laws and regulations applicable to drug development, commercialization or reimbursement;

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

potential infringement or misuse by us of the intellectual property rights of third parties;

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

our ability to issue and sell shares of our common stock under our At-The-Market Issuance Sales Agreement with McNicoll, Lewis & Vlaskovits LLC;

potential ownership changes under Internal Revenue Code Section 382; and

the timeliness and accuracy of information filed with the SEC by third parties.

In addition, the words anticipates, believes, estimates, expects, intends, may, plans, projects, will, and other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. We have included important factors in the cautionary statements included in this prospectus and the documents incorporated by reference in this prospectus, particularly in the sections entitled Risk Factors, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statements.

USE OF PROCEEDS

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

Table of Contents**RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERENCE SECURITY DIVIDENDS**

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

	Fiscal Year Ended					Nine Months
	December 31,					Ended
	2008	2009	2010	2011	2012	September 30,
						2013
Ratio of earnings available to combined fixed charges and preferred stock dividends(1)		18.64				

(1) Due to our losses in years ended December 31, 2008, 2010, 2011, and 2012 and the nine months ended September 30, 2013, the ratio coverage was less than 1:1. Additional earnings of \$56.4 million, \$49.5 million, \$47.9 million, \$40.4 million and \$40.2 million would have been required in each of those periods, respectively, to achieve a coverage of 1:1.

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

interest expense; and

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

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our authorized capital stock consists of 91,500,000 shares. Those shares consist of 81,500,000 shares designated as common stock, \$0.001 par value, and 10,000,000 shares designated as preferred stock, \$0.001 par value. As of November 5, 2013, there were 29,511,041 shares of common stock issued and outstanding.

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

Common Stock

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Upon any liquidation, dissolution or winding up of our business, the holders of common stock are entitled to share equally in all assets available for distribution after payment of all liabilities and provision for liquidation preference of shares of preferred stock then outstanding. Holders of common stock have no preemptive

rights or rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. Holders of common stock are entitled to receive dividends declared by the board of directors, out of funds legally available for the payment of dividends, subject to the rights of holders of preferred stock. Currently, we are not paying dividends.

Our common stock is listed on The NASDAQ Capital Market under the symbol CYTK. The transfer agent and registrar for our common stock is Computershare. Computershare's address is P.O. Box 43078, Providence, RI, 02940.

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

Preferred Stock

Pursuant to our restated certificate of incorporation, our board of directors has the authority, without further approval by our stockholders, to designate and issue up to 10,000,000 shares of preferred stock in one or more series. Our board of directors previously designated 8,070 of the authorized shares of preferred stock as Series A convertible preferred stock, and 23,026 of the authorized shares of preferred stock as Series B convertible preferred stock, none of which are currently outstanding. Our board of directors may designate the powers, preferences and rights, and the qualifications, limitations or restrictions of each series of preferred stock, including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and liquidation preferences, any or all of which may be greater than the rights of the common stock. Thus, without stockholder approval, our board of directors could authorize the issuance of preferred stock with voting, conversion and other rights that could dilute the voting power and other rights of holders of our common stock, and may have the effect of decreasing the market price of the common stock.

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

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

Table of Contents

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

any redemption, repayment or sinking fund provisions;

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

any voting rights;

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

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

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

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

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

a discussion of material U.S. federal income tax consequences, if any.

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

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Anti-Takeover Effects of Some Provisions of Delaware Law

Provisions of Delaware law and our amended and restated certificate of incorporation and amended bylaws could make the acquisition of our company through a tender offer, a proxy contest or other means more difficult and could make the removal of incumbent officers and directors more difficult. We expect these provisions to discourage

coercive takeover practices and inadequate takeover bids and to encourage persons seeking to acquire control of our company to first negotiate with our board of directors. We believe that the benefits provided by our ability to negotiate with the proponent of an unfriendly or unsolicited proposal outweigh the disadvantages of discouraging these proposals. We believe the negotiation of an unfriendly or unsolicited proposal could result in an improvement of its terms.

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

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

the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers, and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

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

Table of Contents

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

Anti-Takeover Effects of Provisions of Our Charter Documents

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

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

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

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

Delaware law provides that stockholders may execute an action by written consent in lieu of a stockholder meeting. However, Delaware law also allows us to eliminate stockholder actions by written consent. Elimination of written consents of stockholders may lengthen the amount of time required to take stockholder actions since actions by

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

DESCRIPTION OF THE WARRANTS

General

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock or preferred stock and may be issued in one or more series. Warrants may be offered independently or in combination with common stock or preferred stock offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

Table of Contents

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

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

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of the warrants;

the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;

the dates on which the right to exercise the warrants shall commence and expire;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

if applicable, a discussion of material U.S. federal income tax considerations;

the antidilution provisions of the warrants, if any;

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

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

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

Holders of warrants will not be entitled to:

vote, consent or receive dividends;

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

exercise any rights as stockholders of Cytokinetics.

Table of Contents

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

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement or free writing prospectus at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant or warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent, if applicable, in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of any warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to any warrant agent.

Upon receipt of the required payment and any warrant certificate properly completed and duly executed at the corporate trust office of any warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by a warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Outstanding Warrants

We have outstanding warrants to purchase 7,692,096 shares of our common stock. Of the outstanding warrants, 1,114,167 will remain exercisable until April 20, 2015 and 6,577,929 will remain exercisable until June 25, 2017. Each outstanding warrant holder is prohibited from exercising the outstanding warrants and obtaining shares of common stock if, as a result of such exercise, the holder and its affiliates would own more than 9.98% of the total

number of shares of our common stock then issued and outstanding.

Table of Contents

PLAN OF DISTRIBUTION

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

through one or more underwriters or dealers;

through agents;

directly to one or more purchasers; or

through a combination of the above.

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

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers as their agents in connection with the sale of the securities. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act of 1933, as amended, which we refer to as the Securities Act. As a result, discounts, commissions or profits on resale received by underwriters, dealers or agents may be treated as underwriting discounts and commissions.

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

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

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

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

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

at market prices prevailing at the time of sale;

at prices related to prevailing market prices; and

at negotiated prices.

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

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

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

Table of Contents

In connection with the offering of the securities, certain persons participating in that offering may engage in transactions that stabilize, maintain or otherwise affect the market price, including over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the common stock in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer is purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

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

Any underwriters who are qualified market makers on the NASDAQ Capital Market may engage in passive market making transactions in the securities on the NASDAQ Capital Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for the security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

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

LEGAL MATTERS

The validity of securities offered hereby will be passed upon by Cooley LLP, Palo Alto, California.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a Registration Statement on Form S-3 under the Securities Act with respect to the shares of common stock we are offering under this prospectus. This prospectus does not contain all of the information set forth in the Registration Statement and the exhibits to the Registration Statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the Registration Statement and the exhibits and schedules filed as a part of the Registration Statement. You may read and copy the Registration Statement, as well as

our reports, proxy statements and other information, at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC's web site at <http://www.sec.gov>.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information we filed with the SEC. This means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus. We incorporate by reference the documents listed below and any future filings (including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement) made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than reports or portions furnished under Items 2.02 or 7.01 of Form 8-K) until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any

Table of Contents

such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

our annual report on Form 10-K for the fiscal year ended December 31, 2012;

the information specifically incorporated by reference into our 2012 Annual Report on Form 10-K referred to above from our definitive proxy statement on Schedule 14A, filed on April 2, 2013;

our quarterly reports on Form 10-Q for the fiscal quarters ended March 31, 2013, June 30, 2013 and September 30, 2013;

our current reports on Form 8-K dated January 25, 2013, February 8, 2013, February 12, 2013, March 11, 2013, March 18, 2013, March 21, 2013, April 1, 2013, May 24, 2013, June 4, 2013, June 12, 2013, June 18, 2013, June 25, 2013, June 25, 2013, July 8, 2013, July 23, 2013, August 22, 2013 and September 23, 2013;

our current reports on Form 8-K dated February 5, 2013, April 30, 2013, July 31, 2013 and October 30, 2013 (in each case, as to information therein explicitly filed with the SEC only); and

the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on March 12, 2004, and any further amendment or report filed hereafter for the purpose of updating any such description.

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

Cytokinetics, Incorporated

280 East Grand Avenue

South San Francisco, California 94080

United States of America

Attn: Investor Relations

(650) 624-3000

Table of Contents

Shares

Common Stock

PROSPECTUS SUPPLEMENT

Cowen and Company

Sole Book-Running Manager

JMP Securities

Lead Manager

February , 2014