CYTOKINETICS INC
Form 10-K
March 06, 2015
Table of Contents

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2014

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
From the transition period from _____ to _____

Commission file number: 000-50633

CYTOKINETICS, INCORPORATED

(Exact name of registrant as specified in its charter)

Delaware	**94-3291317**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
280 East Grand Avenue	
South San Francisco, CA	**94080**
(Address of principal executive offices)	*(Zip Code)*

(650) 624-3000

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, $0.001 par value	The NASDAQ Capital Market

Securities registered pursuant to Section 12(g) of the Act:

None

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

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

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

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes þ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of the Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨ Accelerated filer þ Non-accelerated filer ¨ Smaller reporting company ¨
(Do not check if a smaller reporting company)

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates was $174.5 million, computed by reference to the last sales price of $4.78 as reported by the NASDAQ Market as of the last business day of the Registrant s most recently completed second fiscal quarter, June 30, 2014. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose. The number of shares of common stock held by non-affiliates excluded 106,337 shares of common stock held by directors, officers and affiliates of directors. The number of shares owned by affiliates of directors was determined based upon information supplied by such persons and upon Schedules 13D and 13G, if any, filed with the SEC. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Registrant, that such person is controlled by or under common control with the Registrant, or that such persons are affiliates for any other purpose.

The number of shares outstanding of the Registrant s common stock on February 27, 2015 was 38,674,892 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant s Proxy Statement for its 2015 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission, no later than 120 days after the end of the fiscal year, are incorporated by reference to Part III of this Annual Report on Form 10-K.

Table of Contents

CYTOKINETICS, INCORPORATED

FORM 10-K

Year Ended December 31, 2014

INDEX

Table of Contents

PART I

This report contains forward-looking statements indicating expectations about future performance and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), and the Private Securities Litigation Reform Act of 1995, that involve risks and uncertainties. We intend that such statements be protected by the safe harbor created thereby. Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to, statements about or relating to:

guidance concerning revenues, research and development expenses and general and administrative expenses for 2015;

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 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. 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;

anticipated interactions with regulatory authorities;

the further development of tirasemtiv for the potential treatment of amyotrophic lateral sclerosis (ALS);

the acceptance by regulatory authorities of the effects of tirasemtiv on respiratory function, including slow vital capacity, in patients with ALS as a Phase III clinical trial endpoint to support the registration of tirasemtiv as a treatment for ALS;

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

the potential advancement of omecamtiv mecarbil into Phase III clinical development;

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;

Table of Contents

our ability to protect our intellectual property and 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;

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:

further clinical development of tirasemtiv for the potential treatment of ALS will require significant additional funding and we may be unable to obtain such additional funding on acceptable terms, if at all;

the U.S. Food and Drug Administration (FDA) and/or other regulatory authorities may not accept effects on respiratory function, including slow vital capacity, as an appropriate clinical trial endpoint to support the registration of tirasemtiv for the treatment of ALS;

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

Astellas decisions 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;

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 limit the commercial potential of 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;

Table of Contents

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;

accrual information provided by our contract research organizations and other vendors;

potential ownership changes under Internal Revenue Code Section 382; and

the timeliness and accuracy of information filed with the U.S. Securities and Exchange Commission (the SEC) by third parties.

In addition such statements are subject to the risks and uncertainties discussed in the Risk Factors section and elsewhere in this document. Such statements speak only as of the date on which they are made, and, except as required by law, we undertake no obligation to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

Item 1. ***Business***

Overview

We were incorporated in Delaware in August 1997 as Cytokinetics, Incorporated. We are a clinical stage biopharmaceutical company focused on the discovery and development of novel small molecule therapeutics that modulate muscle function for the potential treatment of serious diseases and medical conditions. Our research and development activities relating to the biology of muscle function have evolved from our knowledge and expertise regarding the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. Our 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 retains exclusive rights to tirasemtiv and is independently developing this drug candidate for the potential treatment of ALS. We have conducted a Phase II clinical trials program for tirasemtiv, including a Phase IIb clinical trial in patients with ALS, known as BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with Tirasemtiv in ALS). Based on the results of BENEFIT-ALS, we are planning to initiate a Phase III clinical development program for tirasemtiv in patients with ALS in 2015. 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 are also developing CK-2127107, a structurally distinct fast skeletal muscle troponin activator, under a strategic alliance with Astellas established in June 2013 and expanded in December 2014. Astellas holds an exclusive license to develop and commercialize CK-2127107 worldwide, subject to our development and commercialization participation rights. Under this strategic alliance, Cytokinetics conducted Phase I clinical trials of CK-2127107 and plans to initiate a Phase II clinical trial of CK-2127107 in patients with spinal muscular atrophy (SMA) in the second half of 2015. CK-2127107 is also being evaluated for potential use in other indications associated with muscle weakness. We are also conducting joint research with Astellas directed to next-generation skeletal muscle activators. Further details regarding our strategic alliance with Astellas can be found below in Item 1 of this report under Research and Development Programs Skeletal Muscle Contractility Program CK-2127107 and Other Skeletal Muscle Activators Astellas Strategic Alliance.

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

Table of Contents

alliance with Amgen. In June 2013, we expanded this 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.

A Phase II clinical trial of omecamtiv mecarbil, known as COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure), is ongoing. COSMIC-HF is designed to assess the pharmacokinetics and tolerability of omecamtiv mecarbil dosed orally in patients with heart failure and left ventricular systolic dysfunction and its effects on echocardiographic measures of cardiac function. 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. We expect to continue our joint research with Amgen directed to next-generation compounds in our cardiac muscle contractility program through 2015. Further details regarding our strategic alliance with Amgen can be found below in Item 1 of this report under Research and Development Programs Cardiac Muscle Contractility Program Amgen Strategic Alliance.

All of our drug candidates have demonstrated evidence of potentially clinically relevant pharmacodynamic activity in humans. In 2015, we expect to continue to focus on translating the observed pharmacodynamic activity of these compounds into potentially meaningful clinical benefits for patients.

Following is a summary of the planned clinical development activities for our drug candidates:

Drug Candidate (Mechanism of Action)	Partnership Status	Potential Indication(s)	Stage of Development	Development Status and Planned Development Activities
Skeletal Muscle Contractility Program				
Tirasemtiv (fast skeletal muscle troponin activator)	Cytokinetics developing independently	ALS	Phase II	We anticipate initiating a Phase III clinical development program for tirasemtiv in patients with ALS in the second quarter of 2015. We anticipate continuing our interactions with regulatory authorities regarding the further development of tirasemtiv throughout 2015.
CK-2127107 (fast skeletal muscle troponin activator)	Partnered with Astellas	SMA	Phase I	We anticipate initiating a Phase II clinical trial in patients with SMA in the second half of 2015. Cytokinetics and Astellas continue to evaluate other indications which may be suitable for CK-2127107 or other skeletal sarcomere activators
Cardiac Muscle Contractility Program				
Omecamtiv mecarbil (cardiac muscle myosin activator)	Partnered with Amgen	heart failure (oral administration)	Phase II	We anticipate the enrollment of patients in the expansion phase of COSMIC-HF to conclude in the first quarter of 2015, and results from COSMIC-HF to be available in the second half of 2015.
Omecamtiv mecarbil		heart failure	Phase II	ATOMIC-HF completed in 2013.

(cardiac muscle myosin activator)	Partnered with Amgen	(IV administration)

Table of Contents

All of our drug candidates have arisen from our cytoskeletal research activities. Our focus on the biology of the cytoskeleton distinguishes us from other biopharmaceutical companies, and potentially positions us to discover and develop novel therapeutics that may be useful for the treatment of severe diseases and medical conditions. Our research and development activities since our inception in 1997 have produced multiple drug candidates that have progressed into clinical testing. Each of these drug candidates has a novel mechanism of action compared to currently marketed drugs, which we believe validates our focus on the cytoskeleton as a productive area for drug discovery. We intend to leverage our experience in muscle contractility in order to expand our current pipeline, and expect to identify additional potential drug candidates that may be suitable for clinical development.

Corporate Strategy

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

Focusing on drug discovery and development activities relating to the biology of muscle function. We intend to capitalize on the knowledge and expertise we have acquired in each of our muscle contractility research and development programs. In these programs, we are investigating potential treatments for diseases or medical conditions where impaired regulation of the contractile function of muscle plays a key role and such diseases or conditions may be amenable to treatment by modulation of muscle contractility, such as heart failure, and medical conditions associated with skeletal muscle weakness or wasting.

Leveraging our cytoskeletal expertise and proprietary technologies to increase the speed, efficiency and yield of our drug discovery and development processes. We believe that our unique understanding of the cytoskeleton and our proprietary research technologies should enable us to discover and potentially to develop drug candidates with novel mechanisms of action that may offer potential benefits not provided by existing drugs and which may have application across a broad array of diseases and medical conditions. We expect that we may be able to leverage our expertise in muscle contractility to expand programs related to other areas of muscle function and which may extend to the potential treatment of other serious medical diseases and conditions. Progressing related programs in parallel may afford us an opportunity to build a broader business that could benefit from multiple products that serve related clinical and commercial needs associated with impaired muscle function, muscle weakness and fatigue. In addition, this strategy may enable us to diversify certain technical, financial and operating risks by advancing several drug candidates.

Focusing on comprehensive development programs that may enhance the success of our activities directed to potential registration. We believe that by focusing on disease areas with well-organized physician-investigator groups, significant unmet clinical needs, and strong patient and disease advocacy, we may enhance our effectiveness in enrolling and conducting clinical trials that may answer important questions about the dosing, tolerability, pharmacokinetics and pharmacodynamics as well as the potential safety and efficacy of our drug candidates. We believe that our considered clinical trial designs and well-executed development programs can improve our ability to realize value from our and our partners clinical development activities. We believe that our investing in these activities may result in more successful later-stage clinical development activities that may increase the likelihood of our achieving our objectives to develop effective therapeutics that may address the needs of patients with grievous diseases and conditions.

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

Table of Contents

commercialization of our drug candidates directed to these markets, we are focusing our activities on a broad range of issues facing patients and payors, including the principal drivers of clinical and economic burdens associated with these diseases. We also seek to focus on opportunities that the multiple constituencies and stakeholders for these markets may recognize as creating value. Accordingly, targeting unmet medical needs in these areas may provide us competitive opportunities and support development of a franchise in diseases involving muscle weakness, wasting and fatigue. In these markets, we believe that a company with limited resources may be able to compete effectively against larger, more established companies with greater financial and commercial resources. For these opportunities, we intend to develop clinical development and sales and marketing capabilities with the goal of becoming a fully-integrated biopharmaceutical company.

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

Research and Development Programs

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

Small molecules that affect muscle contractility may have several applications for a variety of serious diseases and medical conditions. For example, certain diseases and medical conditions associated with muscle weakness may be amenable to treatment by enhancing the contractility of skeletal muscle. Similarly, heart failure is a disease often characterized by impaired cardiac muscle contractility which may be treated by modulating the contractility of cardiac muscle. Because the modulation of the contractility of different types of muscle, such as cardiac muscle and skeletal muscle, may be relevant to multiple diseases or medical conditions, we believe we can leverage our expertise in these areas to more efficiently discover and develop as potential drugs compounds that modulate the applicable muscle type for multiple indications.

We are currently developing a number of small molecule compounds arising from our muscle contractility programs. Tirasemtiv is our lead drug candidate from our skeletal muscle contractility program. Potential indications for which this drug candidate may be useful include skeletal muscle weakness associated with neuromuscular diseases, such as ALS. We have conducted a Phase II clinical trials program for tirasemtiv, and are planning to initiate a Phase III clinical development program of this drug candidate in patients with ALS in the second quarter of 2015. CK-2127107, another drug candidate from this program, is partnered with Astellas world-wide for the potential treatment of SMA and potentially other neuromuscular and non-neuromuscular indications associated with muscle weakness. We have conducted a Phase I clinical trials program for CK-2127107 under this collaboration. We anticipate initiating a Phase II clinical trial of CK-2127107 in patients with SMA in the second half of 2015. Cytokinetics and Astellas continue to evaluate other indications which may be suitable for CK-2127107 or other skeletal sarcomere activators under the collaboration. Omecamtiv mecarbil, a novel cardiac muscle myosin activator, is partnered with Amgen world-wide for the potential treatment of heart failure. Phase II clinical trials have been conducted with both intravenous and oral formulations of omecamtiv mecarbil. An intravenous formulation of omecamtiv mecarbil has been studied in a Phase IIb clinical trial in patients with acute heart failure, and an oral formulation of omecamtiv mecarbil is being studied in a Phase II clinical trial in patients with heart failure.

Table of Contents

We are continuing to conduct discovery, characterization and lead optimization activities for other compounds with the potential to modulate muscle contractility and other muscle functions, such as growth, energetics and metabolism.

Research and Development Expense. Our research and development expenses were $44.4 million, $49.5 million and $35.6 million for 2014, 2013 and 2012, respectively.

Skeletal Muscle Contractility Program

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

We believe that our skeletal sarcomere activators may lead to new therapeutic options for diseases and medical conditions associated with aging, muscle weakness and wasting and neuromuscular dysfunction. The clinical effects of muscle weakness and wasting, fatigue and loss of mobility can range from decreased quality of life to, in some instances, life-threatening complications. By directly improving skeletal muscle function, a small molecule activator of the skeletal sarcomere potentially could enhance functional performance and quality of life in patients suffering from diseases or medical conditions characterized or complicated by muscle weakness or wasting. These may include diseases and medical conditions associated with skeletal muscle weakness or wasting, such as ALS, claudication, myasthenia gravis, sarcopenia (general frailty associated with aging), post-surgical rehabilitation and cachexia in connection with heart failure or cancer.

Tirasemtiv is the lead drug candidate from this program. Cytokinetics retains exclusive rights to tirasemtiv. We have conducted a Phase II clinical trials program for tirasemtiv, and are planning to initiate a Phase III clinical development program for this drug candidate in patients with ALS. We are also developing another drug candidate from this program, CK-2127107, which has been evaluated in Phase I clinical trials in collaboration with Astellas for potential indications associated with muscle weakness. We are planning to conduct a Phase II clinical trial for CK-2127107 in patients with SMA. Tirasemtiv and CK-2127107 are structurally distinct and selective small molecules that activate the fast skeletal muscle troponin complex in the sarcomere by increasing its sensitivity to calcium, leading to an increase in skeletal muscle contractility. Each of tirasemtiv and CK-2127107 has demonstrated pharmacological activity in preclinical models and evidence of potentially clinically relevant pharmacodynamic effects in humans. We are evaluating other potential indications for which tirasemtiv and CK-2127107 may be useful.

Tirasemtiv. Tirasemtiv, a fast skeletal troponin activator, is the lead drug candidate from our skeletal muscle contractility program. We have conducted three evidence of effect Phase IIa clinical trials of tirasemtiv. These evidence of effect clinical trials were randomized, double-blind, placebo-controlled, three-period cross-over studies of single doses of tirasemtiv administered to patients with impaired muscle function. These studies were intended to translate the mechanism of action of tirasemtiv into potentially clinically relevant pharmacodynamic effects. The first of these trials was conducted in patients with ALS, a chronic and progressive disease in which the motor neurons die, thus denervating skeletal muscles and causing them to atrophy. This leads to weakness, fatigue, and eventually complete paralysis and death, primarily from respiratory complications. The second of these trials was conducted in patients with myasthenia gravis, a chronic, autoimmune, neuromuscular disease which is the most common primary disorder of neuromuscular transmission. The third of these trials was conducted in patients with symptoms of claudication, which is pain or cramping in the leg muscles due to inadequate blood flow during exercise, associated with peripheral artery disease. Evidence of potentially clinically relevant pharmacodynamic effects was observed in each of these trials.

In 2014, we completed BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with Tirasemtiv in ALS), a Phase IIb clinical trial of tirasemtiv in patients with ALS. We believe

Table of Contents

the results from BENEFIT-ALS support advancement into Phase III clinical development. We are planning to initiate a Phase III clinical development program for this drug candidate in patients with ALS by the end of 2015.

Tirasemtiv Clinical Development

BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with Tirasemtiv in ALS). In October 2012, we initiated BENEFIT-ALS, a Phase IIb, multi-national, double-blind, randomized, placebo-controlled, clinical trial designed to evaluate the safety, tolerability and efficacy of tirasemtiv in patients with ALS. BENEFIT-ALS enrolled patients in 73 centers in 8 countries. Patients enrolled in BENEFIT-ALS began treatment with open-label tirasemtiv at 125 mg twice daily. Patients who tolerated this open-label treatment for one week were randomized to receive 12 weeks of double-blind treatment with twice-daily oral ascending doses of tirasemtiv or placebo, beginning at 125 mg twice daily and increasing weekly up to 250 mg twice daily (or a dummy dose titration with placebo). Clinical assessments occurred every four weeks during double-blind treatment; patients also returned for follow-up evaluations at one and four weeks after their final dose of double-blind study medication. The primary efficacy analysis of BENEFIT-ALS compared the mean change from baseline in the ALS Functional Rating Scale in its revised form (ALSFRS-R), a clinically validated instrument designed to measure disease progression and changes in functional status, to the average of the scores obtained after 8 and 12 weeks of double-blind treatment on tirasemtiv versus placebo.

In April 2014, BENEFIT-ALS results were presented at the 66th Annual Meeting of the American Academy of Neurology. The trial enrolled 711 patients into the open-label phase of the trial; subsequently, 605 patients were randomized 1:1 to double-blind treatment with either tirasemtiv or placebo. BENEFIT-ALS did not achieve its primary efficacy endpoint, the mean change from baseline in the ALSFRS-R (-2.98 points in the tirasemtiv group versus -2.40 points in the placebo group; $p = 0.11$). Treatment with tirasemtiv resulted in a statistically significant and potentially clinically meaningful reduction in the decline of slow vital capacity (SVC), a measure of the strength of the skeletal muscles responsible for breathing. SVC has been shown to be an important predictor of disease progression and survival in prior trials of patients with ALS. At week 12, the decline in SVC from baseline was -3.12 for patients receiving tirasemtiv versus -8.66 for those receiving placebo ($p < 0.0001$). From week 0 to week 12, the slope of decline in SVC measured as percentage points per day was -0.0394 for patients receiving tirasemtiv versus -0.0905 for those receiving placebo ($p = 0.0006$).

The analyses of other pre-specified secondary efficacy endpoints in BENEFIT-ALS produced mixed results. The muscle strength mega-score, a measure of strength combining the data from several muscle groups in each patient, declined more slowly on tirasemtiv versus placebo. The difference in the rate of decline for sniff nasal inspiratory pressure (SNIP) was not statistically significant); however, SNIP decreased more on tirasemtiv compared with placebo in a statistically significant manner at 4 and 12 weeks. No differences in maximum voluntary ventilation and hand grip fatigue were observed on tirasemtiv versus placebo.

Serious adverse events (SAEs) during double-blind treatment were more frequent on tirasemtiv than on placebo (9.0% vs. 5.4%). The most common SAE was respiratory failure which occurred in 1 patient on tirasemtiv and 3 patients on placebo. Confusional state and delirium occurred in 2 patients on tirasemtiv and no patients on placebo. More patients on tirasemtiv withdrew from the trial following randomization than on placebo (99 vs. 33 patients, respectively). Adverse events more common on tirasemtiv than on placebo (>10% difference) were dizziness, fatigue, and nausea.

Throughout the remainder of 2014, we presented further results from BENEFIT-ALS. These results indicated that:

- Differences in the decline in SVC on tirasemtiv versus placebo observed after 12 weeks of double-blind treatment were maintained for up to 4 weeks after discontinuation of treatment;

- The reduced decline in SVC on tirasemtiv versus placebo was observed consistently across all subgroups of patients in BENEFIT-ALS that were examined;

Table of Contents

The effects of tirasemtiv on SVC were observed at all doses studied and the concentration-response relationship was flat; and

Riluzole did not increase plasma concentrations nor impact the tolerability of tirasemtiv.

Planned Phase III Clinical Development: In October 2014, we announced that we had completed our review of results from BENEFIT-ALS and concluded that effects observed on SVC in patients treated with tirasemtiv were robust and potentially clinically meaningful. We have engaged with regulatory authorities in the U.S. and Europe regarding results from BENEFIT-ALS and plan to advance tirasemtiv into Phase III clinical development. While regulatory interactions are ongoing, we believe that current feedback from these regulatory authorities informs advancement of tirasemtiv to a Phase III clinical development program that is intended to potentially confirm and extend results from BENEFIT-ALS. Key clinical endpoints in the Phase III program will include measures of respiratory function after longer durations of treatment in patients with ALS, including effects on SVC. We have initiated non-clinical and clinical development planning activities for the Phase III program, and anticipate initiating the program in the second quarter of 2015.

Tirasemtiv Strategic and Commercial Planning. During 2014, we made preparations for the potential commercialization of tirasemtiv. These activities included interactions with manufacturers, and corporate development and commercial planning activities to support various scenarios. We expect to continue to engage extensively with ALS experts, both neuromuscular and pulmonary, and with payors, regulatory authorities and patient advocacy groups as we develop plans for the potential commercialization of tirasemtiv as a treatment for patients living with ALS. These commercialization plans will include market assessment and corporate development activities to support the launch of tirasemtiv in the U.S. and Europe, if appropriate.

Background on ALS Market. Limited options exist for the treatment of patients with ALS, which affects as many as 30,000 Americans, with an estimated 5,600 new cases diagnosed each year in the U.S. Based on our primary market research, the per capita prevalence and incidence appears similar in the major European markets. ALS is 20% more common in men than women; however, with increasing age, the prevalence becomes more equal between men and women. The life expectancy of an ALS patient averages two to five years from the time of diagnosis, with 90 to 95% of those diagnosed with ALS having the sporadic form. Of the remaining ALS patient population, 5 to 10% have a family history of the disease (familial ALS). In cases of familial ALS, there is an approximately 50% chance each offspring will develop the disease. The majority of patients with ALS in the U.S. and Europe receive treatment at multidisciplinary centers that specialize in the unique needs of these patients. In the U.S., there are approximately 70 ALS centers of excellence, according to either the ALS Association or the Muscular Dystrophy Association. For most patients with ALS, death is usually due to respiratory failure because of diminished strength in the skeletal muscles responsible for breathing. We believe that the majority of ALS patients in the U.S. and Europe are treated at ALS centers of excellence; therefore, it is a concentrated market. We believe that there is a need for novel therapies to address the urgent unmet medical issues of this patient population which could be addressed by a small, targeted sales force. If tirasemtiv is approved by regulatory authorities in the U.S. or Europe for commercialization for ALS, we believe that these concentrated markets could be an affordable independent commercialization opportunity for Cytokinetics.

CK-2127107 and Other Skeletal Muscle Activators

Astellas Strategic Alliance. CK-2127107 is being developed jointly by Cytokinetics and Astellas. In December 2014, we entered into an Amended and Restated License and Collaboration Agreement with Astellas (the Amended Astellas Agreement). This agreement superseded the License and Collaboration Agreement between Cytokinetics and Astellas of June 2013 (the Original Astellas Agreement). The Amended Astellas Agreement expanded the objective of the collaboration of advancing novel therapies for diseases and medical conditions associated with muscle weakness to include SMA and potentially other neuromuscular indications, in addition to the non-neuromuscular indications provided for in the Original Astellas Agreement.

Table of Contents

Under the Amended Astellas Agreement, we expanded the exclusive license previously granted Astellas under the Original Astellas Agreement to co-develop and commercialize CK-2127107 for potential application in non-neuromuscular indications worldwide to include certain neuromuscular indications as well. Concurrent with the expanded collaboration, the companies agreed to advance CK-2127107 into Phase II clinical development. Cytokinetics will conduct the initial Phase II clinical trial in patients with SMA. We anticipate initiating this trial in the second half of 2015. The development program may include other neuromuscular indications as the companies may agree. Cytokinetics and Astellas will jointly develop and may jointly commercialize CK-2127107 and other fast skeletal troponin activators in neuromuscular indications. Astellas will be responsible for the costs associated with the development of all collaboration products, including CK-2127107, subject to Cytokinetics option to co-fund certain development costs as described below.

Under the Amended Astellas Agreement, the parties extended through 2016 their joint research program to identify next-generation skeletal muscle activators to be nominated as potential drug candidates. This research will be conducted at Astellas expense. Under the Amended Astellas Agreement, Astellas has exclusive rights to co-develop and commercialize CK-2127107 and other fast skeletal troponin activators in SMA and potentially other indications and other novel mechanism skeletal muscle activators in all indications, subject to certain Cytokinetics development and commercialization rights. Cytokinetics may co-promote and conduct certain commercial activities in the U.S., Canada and Europe under agreed scenarios.

Cytokinetics retains an option to conduct early-stage development for certain agreed indications at its initial expense, subject to reimbursement if development continues under the collaboration. Under the Amended Astellas Agreement, Cytokinetics also retains an option to co-promote collaboration products containing fast skeletal muscle activators for neuromuscular indications in the U.S., Canada and Europe, in addition to its option to co-promote other collaboration products in the U.S. and Canada as provided for in the Original Astellas Agreement. Astellas will reimburse Cytokinetics for certain expenses associated with its co-promotion activities. The Amended Astellas Agreement also provides for Cytokinetics to lead certain activities relating to the commercialization of collaboration products for neuromuscular indications in the U.S., Canada and Europe under particular scenarios.

Cytokinetics received an upfront payment of $30.0 million in connection with the execution of the Amended Astellas Agreement. Also, in conjunction with the execution of the Amended Astellas Agreement, we entered into a common stock purchase agreement which provided for the sale of 2,040,816 shares of our common stock to Astellas at a price per share of $4.90 and an aggregate purchase price of $10.0 million, which was received in December 2014. Pursuant to this agreement, Astellas agreed to certain trading and other restrictions with respect to our common stock. Concurrently, Cytokinetics earned a $15.0 million milestone payment relating to Astellas decision to advance CK-2127107 into Phase II clinical development. Cytokinetics is also eligible to potentially receive over $20.0 million in reimbursement of sponsored research and development activities during the next two years of the collaboration. Based on the achievement of pre-specified criteria, Cytokinetics may receive over $600.0 million in milestone payments relating to the development and commercial launch of collaboration products, including up to $112.0 million (of which Cytokinetics has now received $17.0 million) relating to early development of CK-2127107 and for later-stage development and commercial launch milestones for CK-2127107 in non-neuromuscular indications, and over $100.0 million in development and commercial launch milestones for CK-2127107 in each of SMA and other neuromuscular indications. Cytokinetics may also receive up to $200.0 million in payments for achievement of pre-specified sales milestones related to net sales of all collaboration products under the Amended Astellas Agreement. If Astellas commercializes any collaboration products, Cytokinetics will also receive royalties on sales of such collaboration products, including royalties ranging from the high single digits to the high teens on sales of products containing CK-2127107. Cytokinetics also holds an option to co-fund c