Cytokinetics Announces Development Program Update for CK-2127107

October 13, 2014 11:30 AM EDT

Company Completes Program of Five Phase I Clinical Trials Pursuant to Agreed Development Plan with Astellas

South San Francisco, CA, October 13, 2014 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced the completion of five Phase I clinical trials evaluating CK-2127107 in healthy volunteers, and certain other Phase II readiness activities, all in connection with the agreed development plan under the collaboration between Cytokinetics and Astellas Pharma Inc. ("Astellas," Tokyo: 4503). The Phase I clinical trials demonstrated that CK-2127107 appeared safe and well-tolerated in healthy volunteers and that exposures generally increased across dose ranges studied. CK-2127107 increased the response of muscle to neuromuscular input in a dose and plasma concentration related fashion in healthy volunteers consistent with preclinical observations. In addition, an oral tablet formulation of CK-2127107 appears appropriate for use in Phase II clinical trials. These activities were conducted by Cytokinetics in collaboration with Astellas.

"We are pleased to announce the completion of the Phase I clinical trials development program for CK-2127107 and that we have provided data packages to our partners at Astellas from these trials which Cytokinetics conducted in accordance with the collaboration. We believe that these Phase I clinical trials, along with the completed Phase II readiness activities, support the progression of CK-2127107 into later stage development," stated Fady Malik, MD, PhD, Cytokinetics' Senior Vice President, Research and Early Development. "We are looking forward to reviewing these results with our partner Astellas and to jointly defining a potential Phase II development program for CK-2127107."

Phase I Clinical Trials Completed for CK-2127107

Cytokinetics conducted five Phase I clinical trials for CK-2127107 under sponsorship by Astellas. The first Phase I clinical trial, known as CY 5011, was a double-blind, randomized, placebo-controlled study designed to assess the safety, tolerability, and pharmacokinetics of single ascending oral doses of CK-2127107 administered to healthy adult males in a three period, escalating dose, crossover design. The primary objective of this trial was to evaluate the safety and tolerability of single doses of CK-2127107 administered orally to healthy male volunteers. The secondary objective was to evaluate the pharmacokinetic profile of single doses of CK-2127107. Planned single doses of CK-2127107 up to 4000 mg, the highest dose administered in this trial, were well-tolerated without an emerging pattern of adverse events; therefore, a maximum tolerated dose could not be defined. The pharmacokinetic profile of CK-2127107 was linear and dose-proportional across the dose range studied with a mean terminal half-life compatible with once or twice daily dosing.

A second Phase I clinical trial, known as CY 5012, was a double-blind, randomized, placebo-controlled, multiple ascending dose, parallel group study. The primary objective of this clinical trial was to assess the safety, tolerability, and pharmacokinetics of CK-2127107 in healthy young and elderly volunteers. This clinical trial consisted of three ascending dose cohorts of 12 young volunteers (ages 18-55), and two ascending dose cohorts of 12 elderly volunteers (ages 65-85); split evenly between men and women. In each cohort, volunteers received CK-2127107 or placebo in accordance with 2:1 randomization over a 10-day period. This clinical trial demonstrated that a 10-day course of CK-2127107, either 300 mg or 500 mg twice daily, was well tolerated by both younger (18-55 years) and older (65-85 years) subjects. Plasma concentrations of CK-2127107 achieved steady state and no differences in pharmacokinetics between younger and older subjects were observed.

A third Phase I clinical trial, known as CY 5013, was a randomized, placebo-controlled, single dose, 4-period crossover study of CK-2127107 in healthy male volunteers. The primary objective of this clinical trial was to evaluate the change in the force-frequency profile of the tibialis anterior muscle during transcutaneous stimulation of the deep fibular nerve and its relationship to dose and plasma concentrations of CK-2127107. This clinical trial consisted of 16 healthy volunteers who completed four dosing periods administered one week apart. This Phase I clinical trial demonstrated that the response of skeletal muscle to nerve input increased with both the dose and plasma concentration of CK-2127107 and were most evident in the middle of the range of stimulation frequencies tested, consistent with preclinical observations. Compared to pre-dose measurements, statistically significant, placebo-corrected increases in skeletal muscle function were demonstrated at every time point tested after dosing. This clinical trial demonstrated that CK-2127107 amplified the response of muscle to nerve activation following a single dose of CK-2127107 in these subjects and that the results observed in preclinical models were translated into humans.

A fourth Phase I clinical trial, known as CY 5014, was a randomized, open-label, 2-period crossover study designed to assess the relative oral bioavailability, pharmacokinetics, safety and tolerability of two oral formulations of CK-2127107 in healthy volunteers. The primary objective of this clinical trial was to assess the relative oral bioavailability and pharmacokinetic profiles of two formulations of CK-2127107 following a single dose. This clinical trial enrolled 24 healthy male volunteers divided in two cohorts. Each volunteer completed two dosing periods administered one week apart. This Phase I clinical trial demonstrated that single doses of CK-2127107 in suspension, dosed at 300 mg and 1000 mg, were well tolerated by all 25 healthy men enrolled and provided pharmacokinetic data on two different physical forms of CK-2127107 to inform ongoing development of tablet formulations for use in potential future trials.

A fifth Phase I clinical trial, known as CY 5015, was an open-label, randomized, single dose study designed to evaluate the pharmacokinetics, in a fed and fasted state, of an oral tablet formulation of CK-2127107 in healthy male volunteers. The primary objective of this Phase I clinical trial was to assess the relative oral bioavailability and pharmacokinetic profile of CK-2127107 following a single dose and a secondary objective was to evaluate the pharmacokinetic effect of a single dose of CK-2127107 following fed and fasted states. The clinical trial evaluated 24 male volunteers, split evenly into three cohorts, who in a cross-over fashion received two single doses of CK-2127107 administered orally a week apart. Two cohorts received in a fasted state both oral tablet and liquid suspension formulations, in one case at 250 mg and in the other at 1000 mg and one cohort received 500 mg of the oral tablet formulation in both a fasted and fed state. This clinical trial demonstrated that single doses of CK-2127107, administered at doses of 250 mg, 500 mg and 1000 mg, were well tolerated and appeared appropriate for use in potential future clinical trials.

In addition to these five Phase I clinical trials, Cytokinetics has conducted other Phase II readiness activities for CK-2127107 in accordance with an agreed development plan under the joint oversight of Cytokinetics and Astellas. These activities included process improvement and optimization activities for the manufacturing of CK-2127107, pre-clinical and toxicology studies, and Phase II indication prioritization analyses.

Cytokinetics and Astellas Collaboration

Cytokinetics and Astellas entered into a collaboration in June 2013 to advance novel therapies, including CK-2127107, for diseases and medical conditions associated with muscle weakness. Cytokinetics has exclusively licensed to Astellas the rights to co-develop and commercialize CK-2127107 for potential application in non-neuromuscular indications. Cytokinetics is primarily responsible for the conduct of Phase I clinical trials

and certain Phase II readiness activities for CK-2127107 and Astellas will be primarily responsible for the conduct of subsequent development and commercialization activities for CK-2127107. Cytokinetics and Astellas are jointly conducting research in the area of skeletal muscle activation. Astellas has exclusive rights to develop and commercialize other fast skeletal troponin activators in non-neuromuscular indications and to develop and commercialize other novel mechanism skeletal muscle activators in all indications, subject to certain Cytokinetics' development and commercialization rights. Under the collaboration, Cytokinetics is eligible to receive over $450 million in pre-commercialization and commercialization milestones plus royalties.

Background on Skeletal Muscle Activators

Skeletal muscle contractility is driven by the sarcomere, the fundamental unit of skeletal muscle contraction. It is a highly ordered cytoskeletal structure composed of several key proteins. The first, skeletal muscle myosin, is the cytoskeletal motor protein that converts chemical energy into mechanical force through its interaction with a second protein, actin. A set of regulatory proteins, which includes tropomyosin and several types of troponin, make the actin-myosin interaction dependent on changes in intracellular calcium levels. In non-clinical models, CK-2127107 slows the rate of calcium release from the regulatory troponin complex of fast skeletal muscle fibers, which sensitizes the sarcomere to calcium, leading to an increase in skeletal muscle contractility. CK-2127107 and other skeletal sarcomere activators have demonstrated pharmacological activity that may lead to new therapeutic options for diseases associated with aging and muscle wasting. The clinical effects of muscle wasting, fatigue and loss of mobility can range from decreased quality of life to life-threatening complications. By directly improving skeletal muscle function, a small molecule activator of the skeletal sarcomere may potentially enhance physical performance and quality of life in patients with conditions marked by muscle weakness and fatigue.

About Cytokinetics

Cytokinetics 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. Cytokinetics' lead drug candidate from its cardiac muscle contractility program, *omecamtiv mecarbil*, is in Phase II clinical development for the potential treatment of heart failure. Amgen Inc. holds an exclusive license worldwide to develop and commercialize *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. Cytokinetics is independently developing *tirasemtiv*, a fast skeletal muscle activator, as a potential treatment for diseases and medical conditions associated with neuromuscular dysfunction. *Tirasemtiv* is the subject of a Phase II clinical trials program and has been granted orphan drug designation and fast track status by the U.S. Food and Drug Administration and orphan medicinal product designation by the European Medicines Agency for the potential treatment of amyotrophic lateral sclerosis (ALS). Cytokinetics is collaborating with Astellas Pharma Inc. to develop CK-2127107, a skeletal muscle activator structurally distinct from *tirasemtiv*, for non-neuromuscular indications. All of these drug candidates have arisen from Cytokinetics' muscle biology focused research activities and are directed towards the cytoskeleton. The cytoskeleton is a complex biological infrastructure that plays a fundamental role within every human cell. Additional information about Cytokinetics can be obtained at www.cytokinetics.com.

This press release contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics disclaims any intent or obligation to update these forward-looking statements, and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements relating to Cytokinetics' and its partners' research and development activities, including the conduct, design and results of clinical trials, the significance and utility of preclinical data and clinical trial results, and the properties and potential benefits of Cytokinetics' skeletal muscle activators, including CK-2127107, and other drug candidates; and the expected roles of Cytokinetics and Astellas under their collaboration. Such statements are based on management's current expectations, but actual results may differ materially due to various risks and uncertainties, including, but not limited to, further clinical development of tirasemtiv will require significant additional funding, and Cytokinetics may be unable to obtain such additional funding on acceptable terms, if at all; additional Phase I studies of CK-2127107 may be required; potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trials results, patient enrollment for or conduct of clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy, the U.S. Food and Drug Administration or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Astellas' and Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for CK-2127107 and omecamtiv mecarbil, respectively; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; Cytokinetics may be unable to enter into future collaboration agreements for its drug candidates and programs on acceptable terms, if at all; standards of care may change, rendering Cytokinetics' drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.

Contact:

Joanna L. Goldstein
Manager, Corporate Communications & Marketing
(650) 624-3000