



## **Cytokinetics Announces Start of Phase 2 Clinical Trial of CK-2127107 in Patients With Spinal Muscular Atrophy**

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### **Company Initiates Phase 2 Program Under Collaboration With Astellas**

SOUTH SAN FRANCISCO, Calif., Jan. 04, 2016 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK) today announced that its first Phase 2 clinical trial of CK-2127107, a novel fast skeletal muscle troponin activator, in patients with spinal muscular atrophy (SMA) has opened to enrollment. The clinical trial is designed to assess the effect of CK-2127107 on multiple measures of muscle function in both ambulatory and non-ambulatory patients with SMA, a severe, genetic neuromuscular disease that leads to debilitating muscle function and progressive, often fatal, muscle weakness. In collaboration with Astellas (Tokyo Stock Exchange: 4503, "Astellas"), Cytokinetics is developing CK-2127107 as a potential treatment for people living with SMA and certain other debilitating neuromuscular and non-neuromuscular diseases and conditions associated with skeletal muscle weakness and/or fatigue.

The primary objective of this double-blind, randomized, placebo-controlled clinical trial is to determine the potential pharmacodynamic effects of a suspension formulation of CK-2127107 following multiple oral doses in patients with Type II, Type III, or Type IV SMA. Secondary objectives are to evaluate the safety, tolerability and pharmacokinetics of CK-2127107. The trial will enroll seventy-two patients in two sequential, ascending dose cohorts (two cohorts of 36 patients each, half ambulatory and half non-ambulatory). Each cohort will be stratified by ambulatory versus non-ambulatory status to receive CK-2127107 dosed twice daily for 8 weeks.

"Initiating this first Phase 2 trial of CK-2127107 represents a major step forward given our interests to serve the many adolescents and adults who are living with SMA, a disorder with few treatment options," said Robert I. Blum, Cytokinetics' President and Chief Executive Officer. "We look forward to working closely with the investigators and clinical trial sites to evaluate the effects of our next-generation skeletal muscle activator, which we believe holds promise for the potential treatment of patients battling this devastating disease."

#### **Clinical Trial Design**

In this trial, both of the planned ascending dose cohorts will enroll 18 ambulatory (Type III or Type IV) and 18 non-ambulatory patients (Type II or Type III) who are 12 years of age and older and will randomize them 2:1 to receive CK-2127107 or placebo, stratified by ambulatory versus non-ambulatory status. The first cohort of patients will receive 150 mg of CK-2127107 dosed twice daily for eight weeks; the second cohort of patients will receive 450 mg of CK-2127107 dosed twice daily or a lower dose, depending on the data from the first cohort. At the conclusion of the trial, approximately 24 patients will have been randomized to placebo, approximately 24 patients to 150 mg of CK-2127107 twice daily and approximately 24 patients to 450 mg of CK-2127107 twice daily (or a lower dose, pending the review of data from the first cohort). Multiple assessments of skeletal muscle function and fatigability will be performed including respiratory assessments, upper limb strength and functionality for non-ambulatory patients, as well as six-minute walk and timed-up-and-go for ambulatory patients. Additional information can be found at [clinicaltrials.gov](http://clinicaltrials.gov).

#### **About SMA**

SMA is a severe neuromuscular disease that occurs in 1 in every 6,000 to 10,000 live births each year and is one of the most common fatal genetic disorders. Spinal muscular atrophy manifests in various degrees of severity as progressive muscle weakness resulting in respiratory and mobility impairment. There are four types of SMA, named for age of initial onset of muscle weakness and related symptoms: Type I (Infantile), Type II (Intermediate), Type III (Juvenile) and Type IV (Adult onset). Life expectancy and disease severity vary by type of SMA. Type I patients have the worst prognosis, with a life expectancy of no more than 2 years; Type IV patients have a normal life span but eventually suffer gradual weakness in the proximal muscles of the extremities resulting in mobility issues. Few treatment options exist for these patients, resulting in a high unmet need for new therapeutic options to address symptoms and modify disease progression.

#### **About CK-2127107**

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. Skeletal muscle myosin is the cytoskeletal motor protein that converts chemical energy into mechanical force through its interaction with 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. CK-2127107, a novel skeletal muscle activator arising from Cytokinetics' skeletal muscle contractility program, 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 has demonstrated pharmacological activity that may lead to new therapeutic options for diseases associated with muscle weakness and fatigue. In non-clinical models of SMA, a skeletal muscle activator has demonstrated increases in skeletal submaximal muscle force in response to neuronal input and delays in the onset and reductions in the degree of muscle fatigue. CK-2127107 has been the subject of five completed Phase 1 clinical trials in healthy volunteers, which evaluated safety, tolerability, bioavailability, pharmacokinetics and pharmacodynamics.

#### **About Cytokinetics and Astellas Collaboration**

In 2013, Astellas and Cytokinetics formed a partnership focused on the research, development, and commercialization of skeletal muscle activators. The primary objective of the collaboration is to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness. Under the collaboration, Cytokinetics exclusively licensed to Astellas the rights to co-develop and potentially co-commercialize CK-2127107, a fast skeletal troponin activator, in non-neuromuscular indications.

In 2014, Astellas and Cytokinetics agreed to expand the collaboration to include certain neuromuscular indications, including SMA, and to advance CK-2127107 into Phase 2 clinical development, initially in SMA. In connection with the expanded collaboration, the companies also agreed to extend their joint research program through 2016. Under the amended collaboration, Astellas has exclusive rights to co-develop and commercialize CK-2127107 and other fast skeletal troponin activators in non-neuromuscular indications and certain neuromuscular indications (including SMA) 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 North America and Europe under agreed scenarios.

#### **About Cytokinetics**

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to increase muscle function and contractility. Cytokinetics' lead drug candidate is *tirasemtiv*, a fast skeletal muscle troponin activator, for the potential treatment of ALS. *Tirasemtiv* 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 ALS. Cytokinetics retains the right to develop and commercialize *tirasemtiv*. Cytokinetics is collaborating with Amgen Inc. to develop *omecamtiv mecarbil*, a novel cardiac muscle activator, for the potential treatment of heart failure. Cytokinetics is collaborating with Astellas Pharma Inc. to develop CK-2127107, a fast skeletal muscle activator, for the potential treatment of spinal muscular atrophy. Amgen holds an exclusive license worldwide to develop and commercialize *omecamtiv mecarbil* and Astellas holds an exclusive license worldwide to develop and commercialize CK-2127107. Both licenses are subject to Cytokinetics' specified development and commercialization participation rights. For additional information about Cytokinetics, visit <http://www.cytokinetics.com/>.

#### Forward-Looking Statements

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, enrollment and progress of the Phase 2 clinical trial of CK-2127107 in patients with SMA; the significance and utility of preclinical study and clinical trial results; and the properties and potential efficacy and safety profile of CK-2127107 and Cytokinetics' other drug candidates. 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* in ALS patients will require significant additional funding, and Cytokinetics may be unable to obtain such additional funding on acceptable terms, if at all; the FDA and/or other regulatory authorities may not accept effects on slow vital capacity as a clinical endpoint to support registration of *tirasemtiv* for the treatment of ALS; 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 trial 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; Amgen's and Astellas' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *omecamtiv mecarbil* and CK-107, 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.

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