# Cytokinetics Announces Fundamental Research in the Field of Fast Skeletal Muscle Activation Published in the Journal Nature Medicine

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## Novel Mechanistic Approach to Directly Modulating Muscle Contractility May Represent a Promising Strategy to Treat Serious Neuromuscular Disorders

SOUTH SAN FRANCISCO, CA, Mar 05, 2012 (MARKETWIRE via COMTEX) --Cytokinetics, Incorporated (NASDAQ: CYTK) announced today the publication of preclinical research regarding the activation of the troponin complex of fast skeletal muscle by its drug candidate CK-2017357 and the potential therapeutic role that this novel mechanism may play for patients with neuromuscular disorders. This publication in the March 2012 issue of the journal Nature Medicine reveals the mechanism of action for CK-2017357 and the scientific rationale for directly modulating fast skeletal muscle contractility as an innovative therapeutic strategy for improving physical activity in diseases in which neuromuscular function is compromised.

"We are honored to have Cytokinetics' novel scientific research into direct modulators of the skeletal muscle contractile apparatus published in this prestigious journal," stated Fady I. Malik, MD, PhD, FACC, Cytokinetics' Vice President of Biology and Therapeutics and senior author of this report. "This publication summarizes pioneering work performed by our dedicated research team that has supported the progression of CK-2017357 into Phase II clinical development for the potential treatment of patients with neuromuscular diseases."

The publication, titled "Activation of Fast Skeletal Muscle Troponin as a Potential Therapeutic Approach for Treating Neuromuscular Diseases," discusses the potential clinical role for therapies that directly activate troponin in fast skeletal muscle. The authors sought to compensate for the limited neural input which results in muscle weakness, a hallmark of many neuromuscular diseases. CK-2017357, a small-molecule, direct activator of fast skeletal muscle troponin, was developed as a potential pharmacologic treatment intended to increase muscle strength by amplifying the response of muscle when neural input is diminished secondary to neuromuscular disease.

In this publication, the authors demonstrated that CK-2017357 binds selectively to the troponin complex in fast-twitch skeletal muscle and slows the rate of calcium release from Troponin C, thereby sensitizing the muscle to calcium. As a consequence, the force-calcium relationship of the muscle fibers shifted leftwards, as did the force-frequency relationship of a nerve-muscle pair. In both in vitro and in vivo experiments, CK-2017357 increased the production of force at sub-maximal nerve stimulation rates. Notably, in an animal model of myasthenia gravis, sensitization of the fast-twitch skeletal muscle troponin complex to calcium improved muscle force and grip strength immediately after administration of single doses of CK-2017357. The authors concluded that troponin activation may provide a new therapeutic approach to improve physical activity in diseases where neuromuscular function is compromised.

"We believe this novel mechanism of action has the potential to translate into clinically relevant improvements in muscle function and may significantly contribute to enhancing the quality of life for patients suffering from neuromuscular diseases," stated Robert I. Blum, Cytokinetics' President and Chief Executive Officer. "CK-2017357, our first-in-class skeletal troponin activator, has arisen from our scientists' steadfast commitment to research directed to the biology of muscle function and their focus to the discovery and development of potential therapeutic options that may meaningfully improve the lives of patients suffering from seriously debilitating neuromuscular diseases like amyotrophic lateral sclerosis or ALS."

Background on Cytokinetics Skeletal Muscle Contractility Program

Skeletal muscle contractility is driven by the sarcomere, the fundamental unit of skeletal muscle contraction. The sarcomere is a highly ordered cytoskeletal structure composed of skeletal muscle myosin, the cytoskeletal motor that is directly responsible for converting chemical energy into mechanical force, as well as actin, and a set of regulatory proteins, troponins and tropomyosin, which make the actin-myosin interaction dependent on changes in intracellular calcium levels. Cytokinetics' skeletal muscle contractility program is focused to the discovery and development of small molecule skeletal sarcomere activators and leverages Cytokinetics' expertise developed in its ongoing discovery and development of cardiac sarcomere activators, including the cardiac myosin activator omecamtiv mecarbil, now in Phase II clinical development as a potential treatment for heart failure. CK-2017357, a fast skeletal muscle troponin activator, is the lead drug candidate from the company's skeletal muscle contractility program. CK-2017357 selectively activates the fast skeletal muscle troponin complex by increasing its sensitivity to calcium, leading to an increase in skeletal muscle force. This mechanism of action has demonstrated encouraging pharmacological activity in preclinical models that may relate to the potential treatment of diseases associated with aging, muscle wasting or neuromuscular dysfunction. In addition, CK-2017357 has shown pharmacological activity in healthy volunteers, in patients with amyotrophic lateral sclerosis ("ALS"), and in patients with peripheral artery disease and claudication. The clinical effects of muscle 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 may potentially enhance physical performance and quality of life in patients suffering from diseases or medical conditions characterized or complicated by muscle weakness or wasting.

Development Status of CK-2017357 in ALS

Cytokinetics is developing CK-2017357, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or neuromuscular dysfunction. CK-2017357 is currently the subject of a Phase II clinical development program and has been granted orphan-drug designation by the U.S. Food and Drug Administration for the potential treatment of ALS, a debilitating disease of neuromuscular impairment.

CK-2017357 demonstrated potentially clinically relevant pharmacodynamic effects in a Phase IIa Evidence of Effect clinical trial in ALS patients. In that trial, the single doses of CK-2017357 evaluated appeared generally well-tolerated. In addition, both patients and investigators perceived a dose-dependent positive change in the patients' overall status at 6 hours after dosing with CK-2017357, based on a Global Assessment in which the patient and the investigator each independently assessed the patient's status compared to prior to dosing. Furthermore, there was a clear relationship between improvements in Global Assessments and plasma concentrations of CK-2017357 Also at this 6-hour time point, there was a trend towards decreased muscle fatigability, as evidenced by data from a test of sub-maximal hand-grip endurance. Data from that clinical trial also demonstrated a statistically significant increase in the maximum volume of air patients could inhale and exhale (Maximum Voluntary Ventilation) at both 6 and 24 hours after 500 mg of CK-2017357, as well as small but statistically significant increases in maximum strength of certain muscle groups tested.

In December 2011, the company reported data from Part A of its ongoing Phase II clinical trial (CY 4024), in which 24 ALS patients who were not

concurrently taking riluzole were randomized to one of four different treatment groups to receive daily oral doses of placebo or 125 mg, 250 mg, or 375 mg of CK-2017357, respectively, for two weeks. CK-2017357 was well-tolerated by these patients at all dose levels studied. The incidence of dizziness, the most common adverse event, appeared dose-related but was mild in severity in all patients who completed study drug treatment. Most reports of dizziness began early after initiating treatment and resolved spontaneously within the first week of treatment in all but one patient who nevertheless completed the trial No serious adverse events were reported. The second cohort of this clinical trial, or Part B, is ongoing, and is intended to enroll approximately 24 ALS patients who are concurrently taking riluzole; otherwise, Part B is identical in design to Part A. An additional Phase II clinical trial (CY 4025) designed to evaluate the safety and tolerability of an ascending dose-titration regimen of CK-2017357 is also ongoing. Cytokinetics anticipates that results from each of these two clinical trials will be presented at the American Academy of Neurology 64th Annual Meeting in New Orleans, LA on April 25, 2012.

Cytokinetics has met with the U.S. Food and Drug Administration's Center for Drug Evaluation and Research's Division of Neurology Products and with the European Medicines Agency to discuss its progress in the development of CK-2017357 as a potential treatment for patients with ALS and the company's plans for its further development, including potential registration strategies. Cytokinetics is assessing options that may enable the initiation of a registration program for CK-2017357. Cytokinetics anticipates having additional meetings with U.S. and European regulatory authorities during 2012 to discuss the development of CK-2017357 as a potential treatment for patients with ALS, including potential registration strategies.

In July 2010, Cytokinetics was awarded a grant of approximately $2.8 million from the National Institute of Neurological Disorders and Stroke to support research and development of CK-2017357 in myasthenia gravis. The grant was awarded under the American Recovery and Reinvestment Act of 2009. Cytokinetics continues to enroll and dose patients in a Phase IIa Evidence of Effect clinical trial of CK-2107357 in patients with generalized myasthenia gravis. Cytokinetics anticipates that data will be available from this trial in the first half of 2012.

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 (excluding Japan) to develop and commercialize omecamtiv mecarbil and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. Cytokinetics is independently developing CK-2017357, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or neuromuscular dysfunction. CK-2017357 is currently the subject of a Phase II clinical trials program and has been granted orphan-drug designation by the U.S. Food and Drug Administration for the potential treatment of amyotrophic lateral sclerosis, a debilitating disease of neuromuscular impairment in which CK-2017357 demonstrated potentially clinically relevant pharmacodynamic effects in a Phase IIa trial. Cytokinetics is also conducting research of compounds that inhibit smooth muscle contractility and which may be useful as potential treatments for diseases and conditions associated with excessive smooth muscle contraction, such as bronchoconstriction associated with asthma and chronic obstructive pulmonary disorder (COPD). All of these drug candidates and potential drug candidates have arisen from Cytokinetics' 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 plans for and the initiation, conduct, design and results of clinical trials for CK-2017357, the significance and utility of such results, the anticipated timing for the availability of such results and planned presentations of such results, anticipated meetings with regulatory authorities and potential initiation of a registration program for CK-2017357; and the properties and potential benefits of CK-2017357 and Cytokinetics' other drug candidates and potential drug candidates, including CK-2017357's potential utility in the treatment of patients with ALS and myasthenia gravis. 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, 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 (FDA) or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, the FDA may not grant CK-2017357 orphan drug exclusivity in ALS even if it is approved for marketing, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for omecamtiv mecarbil; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products on acceptable terms, if at all; funding from the National Institute of Neurological Disorders and Stroke may not be available in future periods; 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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