



Cytokinetics Announces Fundamental Research in the Field of Cardiac Myosin Activation Published in the Journal Science

March 18, 2011 11:31 AM EDT

Novel Mechanistic Approach to Directly Modulating Muscle Contractility May Represent a Promising Strategy to Treat Systolic Heart Failure

SOUTH SAN FRANCISCO, CA, Mar 18, 2011 (MARKETWIRE via COMTEX) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today the publication of preclinical research in the March 18, 2011 issue of the journal *Science* regarding the activation of cardiac myosin by an investigational drug candidate, omecamtiv mecarbil, and the potential therapeutic role that this novel mechanism may play for patients with systolic heart failure. This publication reveals, for the first time in a peer reviewed journal, the mechanism of action for omecamtiv mecarbil and the scientific rationale for directly modulating cardiac contractility as an innovative therapeutic strategy for improving cardiac performance in patients with heart failure.

"It is our honor to have Cytokinetics' novel scientific research into direct modulators of the cardiac contractile apparatus published in this prestigious journal," stated Fady I. Malik, MD, PhD, FACC, Cytokinetics' Vice President of Biology and Therapeutics and lead author of this report. "This publication summarizes the pioneering work performed by our dedicated research team that has supported the progression of our lead compound, omecamtiv mecarbil, through clinical development and now into Phase IIb clinical trials, which will be conducted by Amgen in collaboration with Cytokinetics."

The publication titled, "Cardiac Myosin Activation: A Potential Therapeutic Approach for Systolic Heart Failure," discusses the potential clinical role for therapies that directly activate cardiac myosin in the treatment of systolic heart failure. The authors recognized that decreased cardiac contractility is a central feature of systolic heart failure and that there is a need for more safe and effective treatment options to improve cardiac contractility. Existing drugs that increase cardiac contractility do so indirectly through signaling cascades but their use is limited by their mechanism-related adverse effects. Omecamtiv mecarbil, a small-molecule, direct activator of cardiac myosin, was developed to address these limitations.

In this publication, the authors demonstrated that omecamtiv mecarbil binds to the myosin catalytic domain and acts by an allosteric mechanism to increase the transition rate of myosin into the strongly actin-bound force-generating state. Paradoxically, omecamtiv mecarbil inhibits adenosine 5'-triphosphate (ATP) turnover in the absence of actin, which suggests that it stabilizes an actin-bound conformation of myosin. In animal models, omecamtiv mecarbil increases cardiac function by increasing the duration of ejection without changing the rates of cardiac contraction. The authors concluded that cardiac myosin activation may provide a new therapeutic approach for patients with systolic heart failure.

"This ground-breaking publication underscores the quality and robustness of the science at our company which relates to the mechanics and biology of muscle function and that serves as the basis for our portfolio of drug candidates," stated Robert I. Blum, Cytokinetics' President and Chief Executive Officer. "Over several years, our promising research has now resulted in multiple first-in-class compounds that may address unmet clinical needs in a broad array of indications and medical conditions associated with impaired muscle contractility."

Development Status of Omecamtiv Mecarbil

Omecamtiv mecarbil, a novel cardiac muscle myosin activator, has been the subject of a clinical trials program comprised of multiple Phase I and Phase IIa trials conducted under Cytokinetics' sponsorship. This program was designed to evaluate the safety, tolerability, pharmacodynamic and pharmacokinetic profiles of both intravenous and oral formulations of omecamtiv mecarbil for the potential treatment of heart failure across the continuum of care, in both hospital and outpatient settings. Two Phase IIa clinical trials of omecamtiv mecarbil from this program have been completed in patients with heart failure. In addition, five Phase I clinical trials of omecamtiv mecarbil were conducted in healthy subjects. Data from each of these trials have been reported previously.

Amgen holds an exclusive, world-wide (excluding Japan) license to omecamtiv mecarbil and related compounds, subject to specified development and commercialization participation rights of Cytokinetics. In February 2011, the company and its partner, Amgen Inc., announced plans to initiate a Phase IIb clinical trial of an intravenous formulation of omecamtiv mecarbil to evaluate its safety and efficacy in patients with left ventricular systolic dysfunction hospitalized for acute heart failure in the first half of 2011.

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 (formerly CK-1827452), is in 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 and non-clinical development 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). In addition, prior Cytokinetics' research generated three anti-cancer drug candidates that have progressed into clinical development: ispinesib, SB-743921 and GSK-923295. 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 the initiation, conduct, design, scope and results of omecamtiv mecarbil clinical trials, the significance and utility of pre-clinical research results for omecamtiv mecarbil, and the potential for cardiac myosin activation as a therapeutic approach for treatment of systolic heart failure; and the properties and potential benefits of omecamtiv mecarbil and Cytokinetics' other drug candidates and potential 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, 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; 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; 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:

Christopher S. Keenan
Director, Investor & Media Relations
(650) 624-3000

SOURCE: Cytokinetics, Inc.