



## **Phase I Clinical Trial Data Relating to Omecamtiv Mecarbil Presented at the 2010 Heart Failure Society of America Annual Meeting**

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### **Investigators Conclude That Omecamtiv Mecarbil Improved Left Atrial Performance in Healthy Volunteers**

SOUTH SAN FRANCISCO, CA, Sep 14, 2010 (MARKETWIRE via COMTEX) --

Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that additional Phase I clinical trial data relating to omecamtiv mecarbil (formerly CK-1827452) was presented as a poster at the 2010 Heart Failure Society of America Annual Meeting being held September 12-15, 2010 at the San Diego Convention Center in San Diego, California.

#### **Poster Presentation**

The poster, titled, "Effect of the Selective Cardiac Myosin Activator, Omecamtiv Mecarbil, on Left Atrial Performance in Healthy Men," was presented on Monday, September 13, 2010 by John R. Teerlink, M.D., F.A.C.C., F.A.H.A., F.E.S.C., Professor of Medicine at the University of California, San Francisco, and Director of the Heart Failure Clinic, Veterans Affairs Medical Center, San Francisco. This new analysis of data from a completed Phase I clinical trial investigated the hypothesis that omecamtiv mecarbil can improve left atrial function in study subjects. In this single-center, double-blind study, 34 healthy men received six-hour infusions on four occasions; each infusion was at least one week apart. Each subject received three ascending doses of omecamtiv mecarbil with a placebo infusion randomized into the treatment sequence. Omecamtiv mecarbil was studied at 10 dose rates ranging from 0.005 to 1 mg/kg/hr. Echocardiograms were obtained at baseline, 1, 3, 6, 7, 8, 10, and 24 hours. In this clinical trial, the protocol-specified maximum tolerated dose of omecamtiv mecarbil was determined to be 0.5 mg/kg/hr administered for 6 hours. Echocardiograms from subjects who received both placebo and omecamtiv mecarbil at 0.5 mg/kg/hr (n=14-16 for the selected variables) were analyzed for left atrial and ventricular volumes, as well as, Doppler blood flows in a blinded fashion. In prior pre-clinical studies and human clinical studies with omecamtiv mecarbil, the most direct evidence of its pharmacologic effect was an increase in left ventricular systolic ejection time. In a similar fashion in this study, the administration of omecamtiv mecarbil increased the duration of atrial systole. This increase in the duration of atrial systole was accompanied by increases in the velocity of blood flow during atrial contraction and in the mitral annular tissue velocity during atrial contraction, supporting the author's conclusion that omecamtiv mecarbil improved left atrial performance in humans.

#### **Development Status of Omecamtiv Mecarbil (formerly CK-1827452)**

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. This program was designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile 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 addition, Cytokinetics conducted five Phase I clinical trials of omecamtiv mecarbil in healthy subjects: a first-time-in-humans study evaluating an intravenous formulation, an oral bioavailability study evaluating both intravenous and oral formulations, and three studies of oral formulations: a drug-drug interaction study, a dose proportionality study and a study evaluating modified-release formulations. Data from each of these trials have been reported previously.

Amgen Inc. holds an exclusive, world-wide (excluding Japan) license to omecamtiv mecarbil, subject to specified development and commercialization participation rights of Cytokinetics' specified development and commercialization participation rights.

#### **Background on Cardiac Myosin Activators and Cardiac Contractility**

Cardiac myosin is the cytoskeletal motor protein in the cardiac muscle cell that is directly responsible for converting chemical energy into the mechanical force resulting in cardiac contraction. Cardiac contractility is driven by the cardiac sarcomere, a highly ordered cytoskeletal structure composed of cardiac myosin, actin and a set of regulatory proteins, and is the fundamental unit of muscle contraction in the heart. The sarcomere represents one of the most thoroughly characterized protein machines in human biology. Current inotropic agents, such as beta-adrenergic receptor agonists or inhibitors of phosphodiesterase activity, increase cardiac cell contractility by increasing the concentration of intracellular calcium, which further activates the cardiac sarcomere. This effect on calcium levels, however, also has been linked to potentially life-threatening side effects. The inotropic mechanism of current drugs also increases the velocity of cardiac contraction and shortens systolic ejection time. In contrast, cardiac myosin activators have been shown to work in the absence of changes in intracellular calcium by a novel mechanism that directly stimulates the activity of the cardiac myosin motor protein. Cardiac myosin activators accelerate the rate-limiting step of the myosin enzymatic cycle and shift the enzymatic cycle in favor of the force-producing state. This inotropic mechanism results not in an increase in the velocity of cardiac contraction, but instead, in a lengthening of the systolic ejection time, which results in increased cardiac contractility and cardiac function in a potentially more oxygen-efficient manner.

#### **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 IIa 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. Cytokinetics is also conducting 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 systemic hypertension or bronchoconstriction. In addition, prior Cytokinetics' research generated three anti-cancer drug candidates that have progressed into clinical development: isipinesib, 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](http://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 significance and utility of clinical trial results, 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

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