Cytokinetics Presents Phase IIa Clinical Trials Data on Omecamtiv Mecarbil at the 2009 Heart Failure Society of America Annual Meeting

September 15, 2009 11:32 AM EDT

Data From Phase IIa Trials Shared at Largest Gathering of U.S. Heart Failure Specialists; Safety and Pharmacodynamic Results Support Progression Into Further Clinical Trials

SOUTH SAN FRANCISCO, CA, Sep 15, 2009 (MARKETWIRE via COMTEX) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that data relating to two Phase IIa clinical trials evaluating omecamtiv mecarbil (formerly CK-1827452), one in stable heart failure patients and one in patients with ischemic cardiomyopathy and angina, were presented in three poster presentations at the 2009 Heart Failure Society of America Annual Meeting in Boston, Massachusetts.

"We are pleased to present these data at the largest annual gathering of heart failure specialists in the United States. Over 5 million people in the United States alone suffer from heart failure, which, despite recent advances in treatment, remains a debilitating disease that increasingly contributes to the medical and economic burdens that are currently the subject of an intense scientific and political debate in our country," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Together with our partner, Amgen, we look forward to progressing omecamtiv mecarbil into additional clinical trials, in order to further evaluate this novel drug candidate in patients with a diagnosis of heart failure."

Poster Presentations

A poster titled, "An Analysis of the Response to CK-1827452, a Selective Cardiac Myosin Activator, in Stable Heart Failure Patients Stratified by Baseline Cardiac Function" was presented on Monday, September 14, by Fady Malik, MD, PhD, FACC, Vice President, Biology and Therapeutics, Cytokinetics, Inc., South San Francisco, California. The primary objective of our clinical trial was to evaluate the safety and tolerability of omecamtiv mecarbil administered as an intravenous infusion to stable heart failure patients. This analysis compared the response to omecamtiv mecarbil in the patient sub-group with more severely depressed cardiac function to those with more preserved cardiac function. The authors concluded that patients with reduced stroke volumes (< 50 mL) at baseline had pharmacodynamic responses to omecamtiv mecarbil that were generally greater than those in patients with greater stroke volumes at baseline, demonstrating pharmacodynamic activity in this more severely affected sub-population of patients from the study. Statistically significant increases in systolic ejection time, stroke volume, cardiac output, fractional shortening, and ejection fraction occurred across the population in a concentration-dependent manner. In addition, the data demonstrated statistically significant correlations between increasing omecamtiv mecarbil plasma concentration and decreases in left ventricular end-systolic volume and left ventricular end-diastolic volume as well as heart rate. The authors concluded that these findings support further study in a larger patient population, and translation of this novel and unique mechanism into higher-risk populations with heart failure.

A poster titlted, "Phase II Safety Study Evaluating the Novel Cardiac Myosin Activator, CK-1827452, in Patients with Ischemic Cardiomyopathy and Angina" was presented on Tuesday, September 15, 2009 by Will Chou, MD, Medical Director, Cytokinetics, Inc., South San Francisco, California. This poster presentation included data from a double-blind, randomized, placebo-controlled Phase IIa clinical trial evaluating the effect of omecamtiv mecarbil on symptom-limited exercise tolerance in heart failure patients with ischemic cardiomyopathy and angina, and included a detailed public disclosure of specific adverse events in the trial. Previously, these data were summarized in a poster presentation at the 2009 Heart Failure Congress of the European Society of Cardiology, held in Nice, France, and at the European Society of Cardiology Congress 2009 held in Barcelona, Spain. The primary safety endpoint of this clinical trial was stopping an exercise treadmill test, performed during double-blind therapy with either omecamtiv mecarbil or placebo, due to angina at a stage earlier than the shorter of two baseline exercise treadmill tests. This endpoint occurred in one patient receiving placebo and in no patients receiving either the lower or higher of two dose levels of omecamtiv mecarbil. The authors concluded that in heart failure patients with ischemic cardiomyopathy and angina, who theoretically could be most vulnerable to the possible deleterious consequences of systolic ejection time prolongation, treatment with omecamtiv mecarbil, at doses producing plasma concentrations previously demonstrated in other trials to increase cardiac function, did not deleteriously affect a broad range of safety assessments in the setting of exercise. The authors concluded that the results of this trial, together with data from previous studies evaluating the pharmacodynamic effects of omecamtiv mecarbil in healthy volunteers and in stable heart failure patients, support further clinical assessments of omecamtiv mecarbil in patients with heart failure.

A poster titled, "Echocardiographic Detection of Increases in Ejection Fraction in Patients with Heart Failure Receiving the Selective Cardiac Myosin Activator, CK-1827452" was presented on Tuesday, September 15, 2009 by Jonathan Goldman, MD, FACC, Chief Medical Officer and Senior Vice President, ICON Medical Imaging, Warrington, Pennsylvania. This poster included three analyses of the effect of omecamtiv mecarbil on ejection fraction. In one analysis, ejection fraction was calculated from two ventricular volumes assessed by the traditional, image-based biplane Method of Discs; in two other analyses, ejection fraction was calculated by each of two different hybrid methods that use a measurement of stroke volume based on Doppler interrogation of the left ventricular outflow tract and a single assessment of ventricular volume by the Method of Discs. In all three analyses, ejection fraction increased with the plasma concentration of omecamtiv mecarbil; however, increases of greater magnitude were observed with the hybrid methods. Ejection fraction assessed by the hybrid methods correlated better with systolic ejection time than did ejection fraction assessed by the Method of Discs. Ejection fraction by the hybrid method based on left ventricular end-systolic volume was slightly better-correlated with systolic ejection time than the hybrid ejection fraction based on left ventricular end-diastolic volume. Recently, these data were presented in a poster format at the European Society of Cardiology Congress 2009 in Barcelona, Spain.

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, and a Phase IIa clinical trial of omecamtiv mecarbil is ongoing. In addition, Cytokinetics has 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.

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' cardiac muscle contractility program is focused on cardiac muscle myosin, a motor protein essential to cardiac muscle contraction. Cytokinetics' lead compound from this program, omecamtiv mecarbil (formerly CK-1827452), a novel small molecule cardiac muscle myosin activator, is in Phase II clinical trials for the potential treatment of heart failure. In May 2009, Amgen Inc. exercised an option to obtain an exclusive worldwide (excluding Japan) license to this program, which includes rights to develop and commercialize omecamtiv mecarbil and related compounds. Under this agreement, Amgen has assumed responsibility for development and commercialization of omecamtiv mecarbil and related compounds, at its expense, subject to specified development and commercialization participation rights of Cytokinetics. In June 2009, Cytokinetics initiated a Phase I clinical trial of CK-2017357, a fast skeletal muscle troponin activator, in healthy volunteers in the United States. CK-2017357 is being developed as a potential treatment for diseases and medical conditions associated with aging, muscle wasting, and neuromuscular dysfunction. In January 2009, Cytokinetics announced the selection of a potential drug candidate directed towards smooth muscle contractility. Cytokinetics' smooth muscle myosin inhibitors have arisen from research focused towards potential treatments for diseases and conditions, such as systemic hypertension, pulmonary arterial hypertension or bronchoconstriction.

Cytokinetics' cancer development programs are focused on mitotic kinesins, a family of motor proteins essential to cell division. Cytokinetics is developing two drug candidates from this program, ispinesib and SB-743921, each an inhibitor of kinesin spindle protein. In addition, Cytokinetics and GlaxoSmithKline are collaborating on research and development activities focused on GSK-923295, an inhibitor of centromere-associated protein E (CENP-E).

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 programs relating to omecamtiv mecarbil and Cytokinetics' other drug candidates and potential drug candidates, including the planned progression of omecamtiv mecarbil into additional clinical trials and the significance of clinical trial results for omecamtiv mecarbil, 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 omecamtiv mecarbil or Cytokinetics' other drug candidates or potential 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, omecamtiv mecarbil or Cytokinetics' other drug candidates or potential 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, conduct, timing and continuation of development activities for omecamtiv mecarbil; GSK's decisions with respect to the design, conduct, timing and continuation of development activities for GSK-923295; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; standards of care may change rendering omecamtiv mecarbil or Cytokinetics' other drug candidates or potential drug candidates obsolete; others may introduce products or alternative therapies for the treatment of indications omecamtiv mecarbil or Cytokinetics' other drug candidates or potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including reimbursements, 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.