



Cytokinetics Announces Interim Clinical Trial Data Relating to CK-1827452 Presented at the European Society of Cardiology Congress 2008

September 2, 2008 11:33 AM EDT

Statistically Significant Improvements in Measures of Cardiac Function Observed in Patients With Stable Heart Failure

SOUTH SAN FRANCISCO, CA, Sep 02, 2008 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that additional interim results from an ongoing Phase IIa clinical trial of CK-1827452 were presented as a poster presentation at the European Society of Cardiology (ESC) Congress 2008, at the Messe Muenchen GmbH in Munich, Germany. The trial is evaluating an intravenous formulation of CK-1827452, a novel cardiac myosin activator being developed for the potential treatment of patients with either acutely decompensated or chronic heart failure. CK-1827452 is the subject of a collaboration and option agreement between Cytokinetics and Amgen Inc.

A poster entitled, "First Clinical Trial of the Selective Cardiac Myosin Activator, CK-1827452, in Heart Failure: Effect of Dose and Plasma Concentration on Systolic Function" was presented by John Cleland, MD, FACC, FRCP, FESC, Professor of Cardiology, Castle Hill Hospital, University of Hull, United Kingdom on September 1, 2008.

The interim analysis included eight patients from each of Cohorts 1 and 2 and six patients from Cohort 3. There were statistically significant correlations between CK-1827452 concentration and increases in systolic ejection time and stroke volume (each $p < 0.0001$), and between CK-1827452 concentration and increases in fractional shortening and cardiac output (each $p < 0.01$). Changes in ejection fraction, left ventricular end-diastolic volume and left ventricular end-systolic volume were not statistically significant. Heart rate declined slightly at the higher concentrations and there were no dose-related changes in blood pressure. Treatments were well tolerated at pre-specified dosages. The authors concluded that CK-1827452 appears to be well-tolerated in stable heart failure patients over a broad range of plasma concentrations during continuous intravenous administration. The authors also concluded that CK-1827452 increases stroke volume, cardiac output, fractional shortening and systolic ejection time in a concentration-dependent manner. In addition, the authors concluded that the observed improvements in systolic function support further study in a larger patient population, and translation of this novel and unique mechanism into populations with more severe and acute heart failure.

"These additional echocardiographic data assist in the interpretation of results previously presented from this ongoing clinical trial and augment our understanding of the novel pharmacodynamic mechanism and encouraging tolerability of CK-1827452," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "We believe that the absence of an increase in left ventricular end-diastolic volume further supports our view that Doppler-derived stroke volume is an accurate and sensitive measure of the effect of CK-1827452 to increase left ventricular systolic function. We look forward to continuing this trial and plan to present additional data at upcoming conferences."

Cytokinetics plans to present interim data from additional patients who have completed treatment in this ongoing trial as part of the Late Breaking Clinical Trials Session at the Annual Meeting of the Heart Failure Society of America in Toronto, Ontario, Canada on September 24, 2008 at 8:30 am ET.

Phase IIa Clinical Trial Design

This Phase IIa clinical trial is a multi-center, double-blind, randomized, placebo-controlled, dose-escalation, pharmacokinetic and pharmacodynamic trial of CK-1827452 in patients with stable heart failure. The primary objective of this trial is to evaluate the safety and tolerability of CK-1827452 administered as an intravenous infusion to stable heart failure patients. The secondary objectives of this trial are to establish a relationship between the plasma concentration and pharmacodynamic effects of CK-1827452 and to determine the pharmacokinetics of CK-1827452 in stable heart failure patients. In addition to routine assessments of vital signs, blood sampling for CK-1827452 levels, and electrocardiographic monitoring, echocardiograms are performed to evaluate cardiac function at various pre-defined time points before, during and after the infusion of CK-1827452.

In this trial, CK-1827452 is administered as an intravenous infusion to cohorts of eight patients each. In each cohort, patients undergo four treatment periods, receiving three escalating active doses of CK-1827452 and one placebo treatment randomized into the dose escalation sequence to maintain blinding. Patients receive a loading infusion to rapidly achieve a target plasma concentration of CK-1827452 during the first hour, followed by a slower one-hour infusion intended to maintain that plasma concentration during the remainder of the infusion. The first two of these cohorts are designed to study a range of target CK-1827452 plasma concentrations, from 90 ng/ml in the lowest dose regimen in Cohort 1 to 650 ng/ml in the highest dose regimen in Cohort 2; Cohort 3 was designed to gain experience across the same range plasma of concentrations, but with infusions of a longer duration. In the first two cohorts, the second, slower, maintenance infusion was continued for one hour; in the third cohort, the maintenance infusion was continued for 23 hours. Following review of safety data from this interim analysis, Cytokinetics opened enrollment in a fourth cohort in this trial. This cohort will also evaluate a one-hour loading infusion followed by 23 hours of maintenance infusions over the same range of target CK-1827452 plasma concentrations evaluated in Cohort 3.

Development Status of CK-1827452

CK-1827452 is currently the subject of a clinical trials program comprised of multiple Phase I and Phase IIa trials. This program is designed to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetic profile of both intravenous and oral formulations of CK-1827452 in a diversity of patients for the potential treatment of heart failure across the continuum of care, in both hospital and outpatient settings.

In June 2008, at the Heart Failure Congress, the annual meeting of the Heart Failure Association of the ESC in Milan, Italy, Cytokinetics announced results from an interim analysis of its first and ongoing Phase IIa clinical trial of CK-1827452 in patients with stable heart failure. At the time of the

analysis, 22 patients had been evaluated in this clinical trial. The safety data from this analysis suggested that CK-1827452 was well-tolerated with no serious adverse events reported in heart failure patients exposed to the intended range of doses and plasma concentrations. A pharmacodynamic-pharmacokinetic analysis of data from these 22 patients showed that when compared to placebo, CK-1827452 produced statistically significant and clinically relevant increases in Doppler-derived stroke volume and fractional shortening as a consequence of statistically significant prolongations of systolic ejection time. In this interim analysis, statistically significant correlations were observed between the increases in the three indices of cardiac ventricular function and increases in the plasma concentration of CK-1827452. Doppler-derived systolic ejection time and stroke volume measured during the second hour of infusion were the most sensitive indicators of effect. Changes in left ventricular ejection fraction, a measurement with high variability in patients with ventricular disease, did not reach statistical significance in that dataset. Across the range of plasma concentrations evaluated, the pharmacokinetics of CK-1827452 were generally linear with respect to dose and similar to those observed in the healthy volunteers in the first-time-in-humans Phase I trial of CK-1827452. Heart rate declined slightly at the higher concentrations and there were no dose-related changes in blood pressure in this interim analysis.

In August 2008, Cytokinetics announced that the company had opened enrollment in Cohort 2 in a second Phase IIa clinical trial that is evaluating CK-1827452 in patients with ischemic cardiomyopathy and angina, based on the Safety Review Committee's recommendation following its review of safety data from Cohort 1. This double-blind, randomized, placebo-controlled Phase IIa clinical trial is designed to evaluate both intravenous and oral formulations of CK-1827452 in patients with ischemic cardiomyopathy and angina. The primary objective of this trial is to assess the effect of intravenous CK-1827452 on symptom-limited treadmill exercise tolerance. The secondary objective of this trial is to assess the tolerability and resulting plasma concentrations of CK-1827452 administered as an oral formulation. The trial is designed to evaluate two cohorts of 45 patients each with ischemic cardiomyopathy and angina and an ejection fraction of less than or equal to 35 percent.

In addition to these two ongoing Phase IIa clinical trials, in April 2008, Cytokinetics opened enrollment in an open-label, non-randomized Phase IIa clinical trial designed to evaluate an intravenous formulation of CK-1827452 administered to patients with stable heart failure undergoing clinically indicated coronary angiography in a cardiac catheterization laboratory. Cytokinetics has conducted five Phase I clinical trials of CK-1827452 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. Cytokinetics' cardiovascular program is focused towards the discovery and development of small molecule cardiac myosin activators in order to create next-generation treatments to manage acute and chronic heart failure. Cytokinetics' program is based on the hypothesis that activators of cardiac myosin may address certain mechanistic liabilities of existing positive inotropic agents by increasing cardiac contractility without increasing intracellular calcium. 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 contractility 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 output in a potentially more oxygen-efficient manner.

About Cytokinetics

Cytokinetics is a biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule drugs that may address areas of significant unmet clinical needs. Cytokinetics' cardiovascular disease program is focused to cardiac myosin, a motor protein essential to cardiac muscle contraction. Cytokinetics' lead compound from this program, CK-1827452, a novel small molecule cardiac myosin activator, entered Phase II clinical trials for the treatment of heart failure in 2007. Under a strategic alliance established in 2006, Cytokinetics and Amgen Inc. are performing joint research focused on identifying and characterizing activators of cardiac myosin as back-up and follow-on potential drug candidates to CK-1827452. Amgen has obtained an option for an exclusive license to develop and commercialize CK-1827452, subject to Cytokinetics' development and commercial participation rights. Cytokinetics' cancer program is focused on mitotic kinesins, a family of motor proteins essential to cell division. Under a strategic alliance established in 2001, Cytokinetics and GlaxoSmithKline (GSK) are conducting research and development activities focused on the potential treatment of cancer. Cytokinetics is developing two novel drug candidates that have arisen from this program, ispinesib and SB-743921, each a novel inhibitor of kinesin spindle protein (KSP), a mitotic kinesin. Cytokinetics is sponsoring a Phase I/II clinical trial of ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer. In addition, Cytokinetics is conducting a Phase I/II trial of SB-743921 in patients with non-Hodgkin or Hodgkin lymphomas. GSK has obtained an option for the joint development and commercialization of ispinesib and SB-743921. Cytokinetics and GSK are conducting collaborative research activities directed to the mitotic kinesin centromere-associated protein E (CENP-E). GSK-923295, a CENP-E inhibitor, is being developed under the strategic alliance by GSK; GSK began a Phase I clinical trial with GSK-923295 in 2007. In April 2008, Cytokinetics announced the selection of a potential drug candidate directed towards skeletal muscle contractility which may be developed as a potential treatment for skeletal muscle weakness associated with neuromuscular diseases or other conditions. 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 Safe Harbor for forward-looking statements contained in the Act. Examples of such statements include, but are not limited to, statements relating to Cytokinetics' research and development programs, including the design, enrollment, conduct and results of clinical trials and planned presentations relating to clinical trial results, and the properties and potential benefits of CK-1827452 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 approval or production of CK-1827452 or Cytokinetics' other drug candidates that could slow or prevent clinical development, 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, including without limitation, due to political instability in countries where clinical trials of CK-1827452 or Cytokinetics' other drug candidates are being conducted, 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; 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; others may introduce products or alternative

therapies for the treatment of indications CK-1827452 or Cytokinetics' other drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from Cytokinetics' partners, including milestones and royalties on future potential product sales under its 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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