



Cytokinetics Announces the Initiation of Third Phase IIa Clinical Trial of CK-1827452

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First Patient Dosed in a Clinical Trial Evaluating the Potential Effects of CK-1827452 on Cardiac Function, Hemodynamics and Oxygen Consumption in Patients With Stable Heart Failure

SOUTH SAN FRANCISCO, CA, Sep 05, 2008 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today the initiation of its third Phase IIa clinical trial evaluating CK-1827452, a novel cardiac myosin activator being developed by the company 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.

This open-label Phase IIa clinical trial is designed to evaluate an intravenous formulation of CK-1827452 in patients with stable heart failure undergoing clinically indicated coronary angiography in the cardiac catheterization laboratory. The primary objective of this trial is to evaluate the potential effects of CK-1827452 on myocardial efficiency, defined as the ratio of ventricular performance to myocardial oxygen consumption. The secondary objectives of this trial are to measure the potential effects of CK-1827452 on ventricular performance, myocardial oxygen consumption, hemodynamics, pressure-volume relationships and systolic ejection time.

Preclinical studies have suggested that CK-1827452 increases ventricular performance in the absence of substantial changes in myocardial oxygen consumption, thereby increasing myocardial efficiency. This trial of CK-1827452 is designed to investigate this finding further in patients with stable heart failure. The protocol for this clinical trial provides for the enrollment of two cohorts of patients. The first cohort, consisting of six patients, will undergo a dose escalation phase, beginning with a target plasma concentration of approximately 280 ng/mL. Based on the tolerability and pharmacodynamic effects observed in this initial cohort, the investigators will select a single dosing regimen to administer to the second cohort, consisting of twelve patients.

"This clinical trial is a significant step towards a fuller understanding of the effects of CK-1827452 in patients with heart failure," stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Because of its novel mechanism, this drug candidate has the potential to demonstrate properties in this trial that could differentiate it from existing inotropic drugs."

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 September 2008, Cytokinetics announced positive results from an interim analysis of its first and ongoing Phase IIa clinical trial of CK-1827452 in patients with stable heart failure. 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, and between CK-1827452 concentration and increases in fractional shortening and cardiac output. 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. CK-1827452 appeared to be well-tolerated in stable heart failure patients over a broad range of plasma concentrations during continuous intravenous administration and CK-1827452 appeared to increase stroke volume, cardiac output, fractional shortening and systolic ejection time in a concentration-dependent manner.

In April 2008, Cytokinetics initiated a Phase IIa trial that is designed to evaluate an intravenous formulation together with an oral formulation of CK-1827452 in patients with ischemic cardiomyopathy and angina. The primary objective of this double-blind, randomized, placebo-controlled Phase IIa clinical 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 August 2008, Cytokinetics opened enrollment in Cohort 2 of this trial, based on the Safety Review Committee's recommendation following its review of safety data from Cohort 1.

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 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 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 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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