Cytokinetics Announces Presentation of Data on Selective Cardiac Myosin Activator CK-1827452 at the 2007 Annual Heart Failure Society of America Meeting

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SOUTH SAN FRANCISCO, CA, Sep 18, 2007 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that two poster presentations related to CK-1827452, a novel small molecule activator of cardiac myosin, were presented at the 2007 Annual Heart Failure Society of America (HFSA) Meeting in Washington, DC. CK-1827452 is being evaluated in clinical trials for the potential treatment of heart failure and is the subject of a Collaboration and Option Agreement between Cytokinetics and Amgen Inc.

Poster Presentations and Discussion at HFSA

The first poster presentation entitled, "Systolic Ejection Time is a Sensitive Indicator of Left Ventricular Systolic Function During Treatment with the Selective Cardiac Myosin Activator CK-1827452," was presented on Monday, September 17, 2007. This poster presentation provided additional data and analysis regarding a first-time-in-human clinical trial, the results of which were initially presented at the 2006 Annual HFSA Meeting in Seattle, WA. The objective of this analysis was to evaluate the concentration-response relationship of CK-1827452 on left ventricular function in healthy volunteers. The authors concluded that CK-1827452 increased left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) over a range of well-tolerated plasma concentrations. In addition, it was determined that systolic ejection time (SET) was the most sensitive marker of drug effect and that increases in LVEF and LVFS were well correlated with increases in SET. SET is easily measured and may serve as a useful indicator of drug effect in patients with heart failure.

The second poster presentation entitled, "Oral Bioavailability of the Selective Cardiac Myosin Activator CK-1827452: Chronic Oral Inotropic Therapy for Heart Failure?" was presented on Tuesday, September 18, 2007. This poster presentation summarized the results of a clinical trial designed to determine the oral bioavailability of CK-1827452 administered as a liquid form and as a solid capsule formulation in both fasted and fed situations versus a reference intravenous infusion. The authors concluded that the absolute bioavailability of CK-1827452 approached 100% for all formulations administered in this clinical trial. The near complete absolute bioavailability suggested that there is little or no first-pass metabolism of this drug candidate. In addition, food did not have a substantial effect on bioavailability but appeared to delay drug absorption in some subjects. CK-1827452, in both oral and intravenous formulations, was well-tolerated with no significant safety issues.

"These poster presentations provide further support for the potential role of CK-1827452 in the treatment of patients with both acute and chronic 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. "These data continue to inform and support our development activities related to CK-1827452 which is being investigated across the continuum of care for heart failure patients."

Development Status of CK-1827452

CK-1827452 is currently the subject of a Phase II clinical trials program. In April 2007, the company announced the initiation of the first Phase IIa clinical trial for CK-1827452, a multi-center, double-blinded, randomized, placebo-controlled, dose-escalation trial which is designed to evaluate the safety, tolerability, pharmacodynamic and pharmacokinetic profile of an intravenous formulation 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 plasma concentration and pharmacodynamic effect for CK-1827452 and to determine the pharmacokinetics of CK-1827452 in stable heart failure patients. In addition to routine assessments of vital signs, blood samples and ECG monitoring, echocardiograms will be performed to evaluate cardiac function at various pre-defined time points.

Data from the first-in-human Phase I clinical trial of CK-1827452 administered intravenously were previously announced at the Heart Failure Society of America annual meeting in September 2006 and the American Heart Association Scientific Sessions in November 2006. This clinical trial demonstrated that the maximum tolerated dose (MTD) was 0.5 mg/kg/hr for the six-hour infusion in healthy volunteers. At this dose, the six-hour infusion of CK-1827452 produced a statistically significant increase in left ventricular ejection fraction as compared to placebo ($p < 0.0001$). At the same dose, CK-1827452 also produced a statistically significant increase in fractional shortening versus placebo ($p < 0.0001$). Underlying these increases in indices of left ventricular function was a lengthening of the systolic ejection time ($p < 0.0001$). These mean changes in ejection fraction, fractional shortening and systolic ejection time were dose-proportional across the range of doses evaluated in this clinical trial. In addition, CK-1827452 exhibited generally linear, dose-proportional pharmacokinetics across the range of doses studied. At the MTD of 0.5 mg/kg/hr for six hours and below, CK-1827452 was well-tolerated when compared to placebo.

The adverse effects at intolerable doses in humans appeared similar to the adverse findings observed in the preclinical safety studies which occurred at similar plasma concentrations. These effects are believed to be related to an excess of the intended pharmacologic effect, resulting in excessive prolongation of the systolic ejection time, and resolved promptly with discontinuation of the infusions of CK-1827452. Pharmacokinetic data from this completed Phase I clinical trial suggested that the half-life of CK-1827452 was sufficient to support development of an oral dosing formulation.

In December 2006, Cytokinetics announced the results of a Phase I oral bioavailability study which were further described during a poster session at the 2007 Heart Failure Society of America Annual Meeting as detailed above. Analysis of the combined pharmacokinetic data from this oral bioavailability study and from the first-in-human study (in which healthy volunteers received intravenous CK-1827452) supports dosing CK-1827452 both intravenously and orally without requiring adjustment for patient weight. Two additional Phase I clinical trials of CK-1827452 have been initiated. The first clinical trial is a Phase I single-center, open-label, sequential, parallel group clinical trial designed to evaluate the potential for certain drug-drug interactions with CK-1827452. The second Phase I clinical trial is a single-center study which is planned to progress from a single-blind, single-dose phase to a randomized double-blind, placebo-controlled, multi-dose phase to evaluate the pharmacokinetics of an oral formulation of CK-1827452 in healthy volunteers.

Background on Amgen Collaboration

In January 2007, Cytokinetics and Amgen announced a strategic collaboration to discover, develop and commercialize novel small-molecule therapeutics that activate cardiac muscle contractility for potential applications in the treatment of heart failure. In addition, Amgen obtained an option to participate in the future development and commercialization of Cytokinetics' lead drug candidate from its cardiovascular disease program, CK-1827452, and other drug candidates arising from the collaboration. The collaboration is worldwide, excluding Japan. Under the agreement, Cytokinetics received approximately $75 million, comprised of a non-refundable up-front license and technology access fee of $42 million and equity investment of approximately $33 million.

Research activities will focus on identifying and characterizing activators of cardiac myosin as back-up and follow-on potential drug candidates to CK-1827452. During the initial two-year research term, in addition to performing research at its own expense under the collaboration, Cytokinetics will continue to conduct all development activities for CK-1827452, at its own expense, subject to Amgen's option and according to an agreed development plan. Amgen's option is exercisable during a defined period, the ending of which is dependent upon the satisfaction of certain conditions, primarily the delivery of Phase I and Phase IIa clinical trials data for CK-1827452 in accordance with an agreed plan sufficient to support its progression into Phase IIb clinical development. To exercise its option, Amgen would pay a non-refundable exercise fee of $50 million and thereafter would be responsible for development and commercialization of CK-1827452 and related compounds, subject to development and commercial participation rights of Cytokinetics. In addition, Cytokinetics may be eligible to receive pre-commercialization and commercialization milestone payments of up to $600 million on CK-1827452 and other products arising from the research, as well as escalating royalties. Cytokinetics also has the opportunity to earn increased royalties by participating in Phase III development costs. In that case, Cytokinetics could co-promote products in North America and would be expected to play a significant role in the agreed commercial activities. If Amgen elects not to exercise its option on CK-1827452, Cytokinetics may then proceed to independently develop CK-1827452 and the research collaboration would terminate.

Background on the Heart Failure Market

Heart failure is a widespread and debilitating syndrome affecting approximately 5 million people in the United States alone. The high and rapidly growing prevalence of heart failure translates into significant hospitalization rates and associated societal costs. The number of

hospital discharges in the United States identified with a primary diagnosis of heart failure rose from 550,000 in 1989 to over 1 million in 2006. Heart failure is one of the most common primary discharge diagnoses identified in hospitalized patients over the age of 65 in the United States. The annual costs of heart failure in the United States are estimated to be $29.6 billion, including $19.3 billion for inpatient care. According to industry reports, the U.S. market for heart failure drugs was approximately $1.3 billion in 2004. Despite currently available therapies, readmission rates for patients over the age of 65 remain high; as high as 42% within one year of hospital discharge and mortality rates are approximately 60% over the five-year period following a diagnosis of acute heart failure. The limited effectiveness of current therapies points to the need for next-generation therapeutics that may offer improved efficacy without increased adverse events.

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' development efforts are directed to advancing multiple drug candidates through clinical trials to demonstrate proof-of-concept in humans, specifically in the areas of heart failure and cancer. 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, recently entered Phase II clinical trials for the treatment of heart failure in 2007. Under a strategic alliance established in 2006, Cytokinetics and Amgen Inc. plan to conduct research with activators of cardiac myosin in order to identify potential treatments for patients with heart failure. Amgen has obtained an option for the joint development and commercialization of CK-1827452 exercisable during a defined period, the ending of which is dependent on Cytokinetics' conduct of further clinical trials of CK-1827452. 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. The company believes that ispinesib has demonstrated clinical activity in Phase II monotherapy clinical trials in breast cancer, ovarian cancer and non-small lung cancer and plans to conduct additional clinical trials with ispinesib. Cytokinetics is also conducting a Phase I/II trial of SB-743921 in non-Hodgkin's lymphoma. GSK has obtained an option for the joint development and commercialization of ispinesib and SB-743921, exercisable during a defined period. 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, subject to Cytokinetics' option to co-fund certain later-stage development activities and to co-promote the drug candidate in North America. GSK began a Phase I clinical trial with GSK-923295 in 2007. All of these drug candidates have arisen from Cytokinetics' research efforts and are directed towards the cytoskeleton. The cytoskeleton is a complex biological infrastructure that plays a fundamental role within every human cell. Cytokinetics' focus on the cytoskeleton enables it to develop novel and potentially safer and more effective classes of drugs directed at treatments for cancer and cardiovascular disease. 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 the initiation, conduct, scope, focus and results of Cytokinetics' and its partners' research and development activities, including of clinical trials; the potential role and benefits of CK-1827452 and Cytokinetics' other drug candidates and potential drug candidates; and the enabling capabilities of Cytokinetics' biological focus. 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, production and marketing of CK-1827452 or Cytokinetics' other drug candidates that could slow or prevent clinical development, product approval or market acceptance, 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 clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have unexpected 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 and maintain patent or trade secret protection for its intellectual property; potential decisions by GSK to postpone or discontinue development efforts for GSK-923295; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing if necessary; standards of care may change or others may introduce products or alternative therapies for the treatment of indications CK-1827452 or Cytokinetics' other drug candidates and potential drug candidates currently or potentially target; and risks and uncertainties relating to the timing and receipt of funds under Cytokinetics' collaborations. 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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