



Cytokinetics Announces Presentation of Non-Clinical Data Relating to CK-1827452 at the 2008 Annual Scientific Sessions of the American College of Cardiology

March 31, 2008 8:02 PM EDT

Novel Drug Candidate Demonstrates Increase in Left Ventricular Function With No Increase in Myocardial Oxygen Consumption in Canine Model

SOUTH SAN FRANCISCO, CA, Mar 31, 2008 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that an abstract related to non-clinical data for CK-1827452, a novel small molecule activator of cardiac myosin, was presented at the 2008 Annual Scientific Sessions of the American College of Cardiology (ACC) Meeting in Chicago, IL. 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 Presentation at ACC

A poster entitled "A Novel Inotropic Agent That Activates Cardiac Myosin and Increases Cardiac Contractility Without Increasing MVO₂ in Heart Failure With Left Ventricular Hypertrophy" was presented today by You-Tang Shen, MD, University of Medicine and Dentistry of New Jersey, Newark, NJ. The objective of this non-clinical study was to examine the effects of CK-1827452 in dogs with heart failure, either with or without pre-existing left ventricular hypertrophy (LVH).

In this study, the authors observed that in dogs with severe LVH but not heart failure, a bolus followed by an infusion of CK-1827452 produced a sustained and significant increase in ejection time and systolic wall thickening with only transient effects on fractional shortening and stroke volume. After the induction of heart failure, these effects were augmented despite the presence of accompanying LVH. Thus, in dogs with heart failure in the presence of severe LVH, in addition to the increases in ejection time and systolic wall thickening, CK-1827452 produced a sustained increase in fractional shortening and stroke volume. These changes were accompanied by decreases in left ventricular end-diastolic pressure, mean left atrial pressure and heart rate. Importantly, the endocardial to epicardial myocardial blood flow ratio and arterial and coronary sinus oxygen content were unchanged. Thus, overall myocardial oxygen consumption was unaffected even as overall systolic function improved.

The authors concluded that CK-1827452 increased left ventricular function and reduced filling pressures but, in contrast to conventional inotropic agents, did not increase myocardial oxygen consumption or reduce subendocardial blood flow in the setting of heart failure or in heart failure with severe LVH. These findings appear to distinguish CK-1827452 from other inotropic mechanisms and suggest that CK-1827452 may be beneficial for the long-term treatment of patients with heart failure.

"These data, combined with the recently announced interim analysis of Phase IIa data for CK-1827452, set the stage for the initiation of our planned Phase IIa clinical trial designed to evaluate this novel mechanism drug candidate in stable heart failure patients undergoing cardiac catheterization," stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Our plan in this next Phase IIa clinical trial of CK-1827452 is to evaluate cardiac ventricular performance and myocardial oxygen consumption to determine whether these encouraging findings may also be seen in humans."

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. In March 2008, Cytokinetics announced positive results from an interim analysis of an ongoing Phase IIa clinical trial of CK-1827452 in patients with stable heart failure. The safety data from this interim analysis suggest that the drug was well-tolerated with no serious adverse events reported in heart failure patients exposed to the intended range of plasma concentrations. In addition, data from the first two cohorts demonstrated that, when compared to placebo, CK-1827452 produced statistically significant and clinically relevant increases in Doppler-derived stroke volume and fractional shortening in association with statistically significant prolongations of systolic ejection time. Statistically significant correlations were observed between the increases in each of these three indices of cardiac ventricular function and increases in the plasma concentration of CK-1827452. Left ventricular ejection fraction, a measurement with high variability in patients with ventricular disease, also increased with increasing plasma concentrations; however, this increase in left ventricular systolic function did not reach statistical significance in these initial cohorts. 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 and blood pressure remained unchanged in the first two cohorts of the Phase IIa trial. Data from the first two cohorts of this ongoing clinical trial of CK-1827452 will be presented at the Heart Failure Congress the annual meeting of the Heart Failure Association of the European Society of Cardiology, to be held June 14-17, 2008 in Milan, Italy.

In addition to the ongoing Phase IIa trial of CK-1827452, Cytokinetics plans to initiate two additional Phase IIa clinical trials of CK-1827452. The first is designed to evaluate an intravenous form of CK-1827452 in stable heart failure patients undergoing cardiac catheterization and the second is designed to evaluate an intravenous form together with an oral formulation of CK-1827452 in patients with ischemic cardiomyopathy.

Three Phase I clinical trials of CK-1827452 were initiated in 2007. The first trial is a single-center, open-label, sequential, parallel group study designed to evaluate the potential for certain drug-drug interactions with CK-1827452. The second trial is a single-center study which progresses from a single-blind, single-dose phase to a randomized, double-blind, placebo-controlled, multi-dose phase and is designed to evaluate the pharmacokinetics of an oral formulation of CK-1827452 in healthy volunteers. The third trial is a single-center, two-part, open-label study designed to assess the pharmacokinetics, relative bioavailability and the effect of food on three different oral modified release prototypes of CK-1827452.

Data from the first-time-in-humans 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. At the maximum

tolerated dose of 0.5 mg/kg/hr for six hours and below, CK-1827452 was well-tolerated compared to placebo. The adverse effects at intolerable doses in humans appeared similar to the adverse findings observed in the preclinical safety studies and 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. CK-1827452 exhibited generally linear, dose-proportional pharmacokinetics across the range of doses studied. Data from this clinical trial demonstrated that a six-hour intravenous infusion of CK-1827452 produced statistically significant increases in Doppler-derived stroke volume, fractional shortening and left ventricular ejection fraction versus placebo in healthy volunteers. Underlying these increases in indices of left ventricular function was a lengthening of the systolic ejection time. These mean changes in stroke volume, ejection fraction, fractional shortening and systolic ejection time were dose-proportional across the range of plasma concentrations evaluated.

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. Analyses of the combined pharmacokinetic data from this oral bioavailability study and from the first-time-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.

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 receive an exclusive license to develop and commercialize Cytokinetics' lead drug candidate from its cardiovascular disease program, CK-1827452, and other drug candidates arising from the collaboration, subject to Cytokinetics' development and commercial participation rights. The license option is for worldwide rights, 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 under the collaboration are focused 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 Cytokinetics' development and commercial participation rights. 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 millions of people in the United States. The high and rapidly growing prevalence of heart failure translates into significant hospitalization rates and associated societal costs. In 2004, over 5 million patients carried a diagnosis of chronic heart failure in the United States. Many of these patients with chronic heart failure suffer acute episodes. The number of diagnosed events of acute heart failure was over 4 million in 2004. These numbers are increasing due to the aging population and an increased likelihood of survival after acute myocardial infarction. The costs to society and the individual attributable to the prevalence of heart failure are high. The estimated annual direct and indirect costs of heart failure on the nation's health care system are estimated to be \$35 billion in 2008. A portion of that cost comes from heart failure drugs used to treat both chronic and acute heart failure. Sales of drugs to treat heart failure reached over \$1.6 billion in 2004, including \$1.3 billion for chronic heart failure and \$0.3 billion for acute heart failure. Despite currently available therapies, readmission rates for patients remain as 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 chronic 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 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' development efforts are primarily directed to advancing multiple drug candidates through clinical trials with the objective of determining the intended pharmacodynamic effect or effects in two principal diseases: 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, 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 believes that ispinesib has demonstrated clinical activity in Phase II monotherapy clinical trials in breast cancer, ovarian cancer and non-small cell lung cancer and recently initiated an additional 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 on a more dose-dense schedule than previously studied. Cytokinetics is also conducting a Phase I/II trial of SB-743921 on a similar more dose-dense schedule in non-Hodgkin and Hodgkin lymphomas. 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 any resulting approved drug 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 activities 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 within the meaning 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 planned clinical trials; the size and growth of potential markets for drug candidates arising out of Cytokinetics' heart failure program, including for CK-1827452; the potential benefits of CK-1827452 and Cytokinetics' other drug candidates and potential drug candidates; the enabling capabilities of Cytokinetics' cytoskeletal focus; and Cytokinetics' potential receipt of funds and anticipated role in development and commercialization activities under its collaboration and option agreement with Amgen. 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 Cytokinetics' drug candidates, including CK-1827452, 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 take longer than anticipated, 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, Cytokinetics may be unable to obtain and maintain patent or trade secret protection for its intellectual property, GSK may potentially decide 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 the timing and receipt of funds under Cytokinetics' collaborations may be uncertain. 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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