



## Cytokinetics to Present Clinical and Non-Clinical Data on Selective Cardiac Myosin Activator CK-1827452 at the 2006 Annual Heart Failure Society of America Meeting

September 5, 2006 4:00 AM EDT

South San Francisco, CA, September 5, 2006 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced today that the results of a Phase I clinical trial evaluating CK-1827452, a novel small molecule activator of cardiac myosin, in healthy volunteers, along with non-clinical data arising from Cytokinetics' cardiovascular program, will be presented at the 2006 Annual Heart Failure Society of America (HFSA) Meeting in Seattle, Washington.

### Phase I Clinical Data Presentation at HFSA

Late Breaking Abstract: The Selective Cardiac Myosin Activator CK-1827452, a Calcium-Independent Inotrope, Increases LV Systolic Function by Increasing Ejection Time: Results of a First-in-Human Study of a Unique and Novel Mechanism. (Oral Presentation on Wednesday, September 13, 2006, during the Recent and Late Breaking Trials Session, 8:30 a.m. – 10:00 a.m. PT; presentation will be made at 9:15 a.m. by John R. Teerlink, MD, FACC, FAHA, FESC, University of California, San Francisco and Director of the Heart Failure Clinic, Veterans Affairs Medical Center).

### Non-Clinical Poster Presentations and Discussion at HFSA

The abstracts related to these presentations are currently available through the HFSA website ([www.hfsa.org](http://www.hfsa.org)). The posters will be presented at the HFSA meeting during the CV Pharmacology Session as follows:

Abstract #277: In Vitro and In Vivo Characterization of CK-1827452, a Selective Cardiac Myosin Activator. (Poster displayed on Tuesday, September 12, 2006, 9:00 a.m. – 7:00 p.m. PT and Poster Presentation, 5:45 p.m. – 6:45 p.m. PT by Kathleen A. Elias, PhD, Cytokinetics).

Abstract #281: Activating Cardiac Myosin, a Novel Inotropic Mechanism to Improve Cardiac Function in Conscious Dogs with Congestive Heart Failure. (Poster displayed on Tuesday, September 12, 2006, 9:00 a.m. – 7:00 p.m. PT and Poster Presentation, 5:45 p.m. – 6:45 p.m. PT by You-Tang Shen, MD, Department of Cell Biology and Molecular Medicine and Cardiovascular Research Institute, New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, NJ).

Abstract #283: Cardiac Myosin Activator CK-1316719 Increases Myofibril ATPase Activity and Myocyte Contractility in a Rat Model of Heart Failure. (Poster displayed on Tuesday, September 12, 2006, 9:00 a.m. – 7:00 p.m. PT and Poster Presentation, 5:45 p.m. – 6:45 p.m. PT by Robert L. Anderson, Cytokinetics).

### Investor Luncheon and Presentation

Cytokinetics senior management will host an investor luncheon from 12:00 p.m. to 2:00 p.m. PT on Wednesday, September 13, 2006 in the Menzies Room at the Grand Hyatt Seattle, 721 Pine Street, Seattle, Washington to discuss the results of the Phase I clinical trial of CK-1827452. At the luncheon, a panel of speakers will discuss preclinical and Phase I clinical trial data with CK-1827452 and provide commentary on CK-1827452 and trends in the treatment of heart failure. The panel will include Fady Malik, MD, PhD, FACC, Director of Cardiovascular Programs at Cytokinetics, Barry Massie, MD, FACC, Professor of Medicine at the University of California, San Francisco and Chief of Cardiology at the Veterans Affairs Medical Center in San Francisco, John R. Teerlink, MD, FACC, FAHA, FESC, Associate Professor of Medicine at the University of California, San Francisco and the Director of the Heart Failure Clinic at the Veterans Affairs Medical Center, San Francisco, and Andrew A. Wolff, MD, FACC, Senior Vice President of Clinical Research and Development and the Chief Medical Officer at Cytokinetics. The panel presentation and discussion will be simultaneously webcast beginning at 12:30 p.m. and can be accessed in the Investor Relations section of Cytokinetics' website at [www.cytokinetics.com](http://www.cytokinetics.com). The live audio of the forum is also accessible via telephone to investors, members of the news media and the general public by dialing either (866) 578-5771 (United States and Canada) or (617) 213-8055 (International) and typing in the passcode 82325202.

An archived replay of the webcast will be available via Cytokinetics' website until September 27, 2006. The replay will also be available via telephone from September 13, 2006 at 2:30 p.m. Pacific Time until September 27, 2006 by dialing (888) 286-8010 (United States and Canada) or (617) 801-6888 (International) and typing in the passcode 56551325.

### Development Status of CK-1827452

A Phase I, first-in-humans clinical trial designed to evaluate CK-1827452, a novel, small-molecule, direct activator of cardiac myosin, has recently been completed with an intravenous formulation in healthy volunteers. The clinical activity of CK-1827452 in that clinical trial is consistent with results from preclinical models which evaluated this drug candidate in both normal dogs and dogs with heart failure. In these preclinical models, underlying the increase in ejection fraction and fractional shortening was a dose-related increase in the systolic ejection time, which has now also been observed in humans. Data presented at the 2005 Annual Meeting of the Heart Failure Society of America from a dog model of heart failure demonstrated that CK-1827452, administered as a 0.5 mg/kg bolus followed by a 3-4 hour infusion at 0.5 mg/kg/hr, increased cardiac contractility and cardiac output without increasing myocardial oxygen consumption. Preclinical studies have also demonstrated more pronounced effects of CK-1827452 on indices of cardiac function in dogs with heart failure compared to effects achieved in normal dogs.

Cytokinetics initiated a Phase I clinical trial to evaluate the pharmacokinetic profile of CK-1827452 when administered orally in August of 2006 and expects that CK-1827452 will be entering an international Phase II clinical trials program in patients with heart failure in the second half of 2006. This program is planned to evaluate CK-1827452 in a diversity of patients including those with stable heart failure, inducible ischemia, impaired renal function and acute heart failure. This program is designed to test the safety and efficacy of CK-1827452, in both intravenous and oral formulations, for the potential treatment of heart failure across the continuum of care, both in the hospital and the outpatient settings.

**Background on the Heart Failure Market** Heart failure is a widespread and debilitating syndrome affecting approximately five 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 2003. 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 \$1.33 billion in 2004. Despite currently available therapies, readmission rates for patients over the age of 65 remain high at 30 to 40 percent within six months of hospital discharge and mortality rates exceed 50% 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, which may be associated with adverse clinical effects in heart failure patients. 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 indirectly activates cardiac myosin; 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 calcium-independent 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 specifically target 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, cardiovascular disease and other diseases. Under a strategic alliance established in 2001, Cytokinetics and GlaxoSmithKline (GSK) are collaborating to develop and commercialize small molecule therapeutics targeting human mitotic kinesins for applications in the treatment of cancer and other diseases. Ispinesib (SB-715992), SB-743921 and GSK-923295 are being developed under the strategic alliance with GSK. GSK is conducting Phase II and I<sub>b</sub> clinical trials for ipinesib and a Phase I clinical trial for SB-743921, and Cytokinetics is conducting a Phase I/II trial of SB-743921 in non-Hodgkin's lymphoma. Cytokinetics' unpartnered cardiovascular disease program is the second program to leverage the company's expertise in cytoskeletal pharmacology. Cytokinetics recently completed a Phase I clinical trial with CK-1827452, a novel small molecule cardiac myosin activator, for the intravenous treatment of heart failure and also is advancing CK-1827452 as a potential drug candidate for the treatment of chronic heart failure via oral administration. Additional information about Cytokinetics can be obtained at <http://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 about the timing, scope and focus of Cytokinetics' clinical research and development activities with respect to CK-1827452, and presentations of data and results with respect to such activities,, the size and growth of expected markets for CK-1827452, the 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 factors. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to difficulties or delays in patient enrollment for clinical trials, unexpected adverse side effects or inadequate therapeutic efficacy of CK-1827452 or Cytokinetics' other drug candidates and other potential difficulties or delays in 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 the risks relating to uncertainty of patent protection for Cytokinetics' intellectual property or trade secrets, Cytokinetics' ability to obtain additional financing if necessary and unanticipated research and development and other costs), changing standards of care and the introduction of products by competitors or alternative therapies for the treatment of indications currently or potentially targeted by CK-1827452 and the implementation and maintenance of procedures, policies, resources and infrastructure relating to compliance with new or changing laws, regulations and practices. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.