



## Cytokinetics Announces Heart Failure Program Update

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Jul 26, 2012 (Marketwire via COMTEX) --Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that the company and Amgen have reviewed data arising from a recently completed Phase I clinical trial designed to assess the safety, tolerability and pharmacokinetics of modified release oral formulations of *omecamtiv mecarbil* in healthy volunteers. This clinical trial was conducted by Amgen in collaboration with Cytokinetics. Based on the review of these data, the companies have selected oral formulations of *omecamtiv mecarbil* from this Phase I trial that warrant further evaluation in patients with heart failure. Cytokinetics and Amgen are discussing plans for the initiation of a Phase II clinical trial of these oral formulations. Amgen holds an exclusive worldwide (excluding Japan) license to *omecamtiv mecarbil* and related compounds, subject to specified development and commercialization participation of Cytokinetics.

The Phase I clinical trial was a randomized, open-label, 4-period cross-over study designed to determine the oral bioavailability of multiple modified release oral formulations of *omecamtiv mecarbil* in healthy volunteers. Sixty-five volunteers were enrolled in this study. Each volunteer received two of the six oral formulations included in the study, each administered as a single dose under fasted and fed conditions. The primary objective of this study was to determine the bioavailability of multiple modified release oral formulations of *omecamtiv mecarbil* following single dose administration under fasting conditions and to evaluate the effect of food on bioavailability. The secondary objectives included safety, tolerability and pharmacokinetic profiles of *omecamtiv mecarbil* when administered in multiple oral formulations.

"Following the review of data from this Phase I clinical trial, we are pleased that we were able to identify multiple oral formulations of *omecamtiv mecarbil* that warrant further evaluation in a Phase II trial in patients with heart failure," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "We look forward to working with Amgen to finalize the design of this next Phase II clinical trial that, together with the ongoing Phase IIb clinical trial of an intravenous formulation of *omecamtiv mecarbil*, may inform the potential progression of our novel mechanism drug candidate into later-stage clinical trials."

### Development Status of *Omecamtiv Mecarbil*

*Omecamtiv mecarbil*, a novel cardiac muscle myosin activator, is being evaluated in the ATOMIC-AHF (A Trial of *Omecamtiv Mecarbil* to Increase Contractility in Acute Heart Failure) clinical trial. This Phase IIb clinical trial is an international, multicenter, randomized, double-blind, placebo-controlled study in approximately 600 patients, enrolled in three sequential, ascending-dose cohorts. In each cohort, patients will be randomized to receive intravenous (iv) *omecamtiv mecarbil* or placebo. The primary objective of this trial is to evaluate the effect of iv *omecamtiv mecarbil* administered for 48 hours compared to placebo on dyspnea (shortness of breath) in patients with left ventricular systolic dysfunction hospitalized for acute heart failure. The secondary objectives are to assess the safety and tolerability of three dose levels of iv *omecamtiv mecarbil* compared with placebo and to evaluate the effects of 48 hours of treatment with iv *omecamtiv mecarbil* on additional measures of dyspnea, patients' global assessments, change in N-terminal pro brain-type natriuretic peptide (a biomarker associated with the severity of heart failure) and short-term clinical outcomes in these patients. In addition, the trial will be evaluating the relationship between plasma concentrations of *omecamtiv mecarbil* and echocardiographic parameters in patients with acute heart failure. In May 2012, Cytokinetics announced the opening of the second cohort of ATOMIC-AHF to enrollment.

Prior to the initiation of this Phase IIb clinical trial, *omecamtiv mecarbil* was the subject of a clinical trials program comprised of multiple Phase I and Phase IIa trials conducted under Cytokinetics' sponsorship. This program was designed to evaluate the safety, tolerability, pharmacodynamic and pharmacokinetic profiles of both intravenous and oral formulations of *omecamtiv mecarbil* for the potential treatment of heart failure across the continuum of care, in both hospital and outpatient settings. 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. 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 side effects that are potentially life-threatening. 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 function in a potentially more oxygen-efficient manner.

### About Cytokinetics

Cytokinetics is a clinical-stage biopharmaceutical company focused on the discovery and development of novel small molecule therapeutics that modulate muscle function for the potential treatment of serious diseases and medical conditions. Cytokinetics' lead drug candidate from its cardiac muscle contractility program, *omecamtiv mecarbil*, is in Phase II clinical development for the potential treatment of heart failure. Amgen Inc. holds an exclusive license worldwide (excluding Japan) to develop and commercialize *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. Cytokinetics is independently developing CK-2017357, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or neuromuscular dysfunction. CK-2017357 is currently the subject of a Phase II clinical trials program and has been granted orphan drug designation and fast track status by the U.S. Food and Drug Administration and orphan medicinal product designation by the European Medicines Agency for the potential treatment of amyotrophic lateral sclerosis, a debilitating disease of neuromuscular impairment in which treatment with CK-2017357 produced potentially clinically relevant pharmacodynamic effects in Phase II trials. Cytokinetics is also conducting research on compounds that inhibit smooth muscle contractility and which may be useful as potential treatments for diseases and conditions associated with excessive smooth muscle contraction, such as bronchoconstriction associated with asthma and chronic obstructive pulmonary disease. 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](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 Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements relating to Cytokinetics' and Amgen's research and development activities, including the initiation, conduct, design, scope and results of omecamtiv mecarbil clinical trials, the suitability of the selected modified release oral formulations of omecamtiv mecarbil for further evaluation, and the properties and potential benefits of omecamtiv mecarbil and Cytokinetics' other drug candidates and compounds. 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 approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or 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, 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; Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for omecamtiv mecarbil; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products on acceptable terms, if at all; Cytokinetics may be unable to enter into future collaboration agreements for its drug candidates and programs on acceptable terms, if at all; standards of care may change, rendering Cytokinetics' drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics' 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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