# Cytokinetics Announces Update to Heart Failure Program

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**ATOMIC-AHF Has Completed Patient Enrollment;**

**Dosing of Patients in COSMIC-HF Has Initiated**

***South San Francisco, CA, March 18, 2013 -*** Cytokinetics, Incorporated (Nasdaq: CYTK) announced today that ATOMIC-AHF has completed patient enrollment in its third and final cohort. ATOMIC-AHF (**A**cute **T**reatment with ***O****mecamtiv* ***M****ecarbil* to **I**ncrease **C**ontractility in **A**cute **H**eart **F**ailure) is a Phase IIb clinical trial designed to evaluate the safety, tolerability and efficacy of an intravenous formulation of *omecamtiv mecarbil* compared to placebo in patients with left ventricular systolic dysfunction who are hospitalized with acute heart failure. Cytokinetics expects results from ATOMIC-AHF will be announced in mid-year 2013.

Cytokinetics also announced that dosing of patients has initiated in COSMIC-HF **(C**hronic **O**ral **S**tudy of **M**yosin Activation to **I**ncrease **C**ontractility in **H**eart **F**ailure). COSMIC-HF is a Phase II clinical trial designed to evaluate the pharmacokinetics, safety and efficacy of oral modified release formulations of *omecamtiv mecarbil,* in patients with chronic, stable heart failure and left ventricular systolic dysfunction.

Amgen holds an exclusive, worldwide license (excluding Japan) to *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. ATOMIC-AHF and COSMIC-HF are conducted by Amgen in collaboration with Cytokinetics.

**ATOMIC-AHF: Phase IIb Clinical Trial of Intravenous *Omecamtiv Mecarbil***

ATOMIC-AHF is an ongoing Phase IIb clinical trial designed to evaluate an intravenous formulation of *omecamtiv mecarbil* in approximately 600 patients enrolled in 3 sequential, ascending-dose cohorts. In each cohort, patients will be randomized 1:1 to *omecamtiv mecarbil* or placebo. The primary objective of this trial is to evaluate the effect of 48 hours of intravenous *omecamtiv mecarbil* 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 3 dose levels of intravenous *omecamtiv mecarbil* compared with placebo and to evaluate the effects of 48 hours of treatment with intravenous *omecamtiv mecarbil* on additional measures of dyspnea, patients' global assessments, change in N-terminal pro brain-type natriuretic peptide and short-term clinical outcomes in these patients. In addition, the trial is evaluating the relationship between plasma concentrations of *omecamtiv mecarbil* and these parameters in patients with acute heart failure.

**COSMIC-HF: Phase II Clinical Trial of Oral Forms of *Omecamtiv Mecarbil***

COSMIC-HF is a double-blind, randomized, placebo-controlled, multicenter, dose escalation study designed to assess the pharmacokinetics (PK) and tolerability of three oral modified-release formulations of *omecamtiv mecarbil* in patients with heart failure and left ventricular systolic dysfunction, and to select one of them for further evaluation. During the dose escalation phase, approximately 40 patients will be randomized 1:1:1:1 to placebo or one of three different oral formulations of *omecamtiv mecarbil* in each of two ascending dose PK cohorts to enable selection of one of these oral formulations for the planned expansion phase of the trial. The dose of *omecamtiv mecarbil* will be 25 mg twice daily in the first PK cohort and 50 mg twice daily in the second PK cohort. If necessary, a third PK cohort will evaluate 75 mg twice daily. Following the dose escalation phase of the trial, there is a planned expansion phase of the trial in which approximately 300 patients will be randomized 1:1:1 to receive one oral formulation of *omecamtiv mecarbil* selected from the three studied in the prior ascending dose PK cohorts at one of two dose levels or placebo. The two dose levels of *omecamtiv mecarbil* to be studied in the expansion cohort will be based on the data from the ascending dose PK cohorts. The primary objectives of this study are to select an oral modified-release formulation and dose (or doses) of *omecamtiv mecarbil* for chronic twice-daily dosing in patients with heart failure and left ventricular systolic dysfunction and to characterize its safety, tolerability, and pharmacokinetics after 12 weeks of treatment. The secondary objectives are to assess the changes from baseline in systolic ejection time, stroke volume, left ventricular end-systolic diameter, left ventricular end-diastolic diameter, heart rate and N-terminal pro-brain natriuretic peptide (a biomarker associated with the severity of heart failure) after 12 weeks of treatment.

**Development Status of *Omecamtiv Mecarbil***

In 2012, dosing initiated in a Phase I open-label, single-dose clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of *omecamtiv mecarbil* in patients with various degrees of renal insufficiency, including patients requiring chronic hemodialysis. This trial is conducted by Amgen in collaboration with Cytokinetics. Also, in 2012, Cytokinetics and Amgen reviewed data from a prior Phase I randomized, open-label, 4-period cross-over clinical trial designed to assess the safety, tolerability and pharmacokinetics of multiple oral formulations of *omecamtiv mecarbil* in healthy volunteers. The formulations under evaluation in COSMIC-HF were selected from among those oral formulations.

Prior to the conduct of the ongoing trials including ATOMIC-AHF and COSMIC-HF, *omecamtiv mecarbil* was the subject of a clinical trials program conducted by Cytokinetics and comprised of five Phase I trials in healthy volunteers and two Phase IIa trials in patients with heart failure. Those trials were 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. Data from each of these trials were reported previously.

Additional information about trials of *omecamtiv mecarbil* can be found at www.clinicaltrials.gov.

**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 *tirasemtiv*, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or neuromuscular dysfunction. *Tirasemtiv* 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 *tirasemtiv* produced potentially clinically relevant

pharmacodynamic effects in Phase II trials. All of these drug candidates have arisen from Cytokinetics' muscle biology focused 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 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 progress, conduct, design and results of clinical trials, the significance and utility of clinical trial results, and the properties and potential benefits of omecamtiv mecarbil 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 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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