



## Cytokinetics Provides Development Program Update for Omecamtiv Mecarbil

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***Over 275 Patients Enrolled in COSMIC-HF; Data Monitoring Committee Recommends Continuation with No Changes to the Protocol***

### ***Phase I Pharmacokinetic and Safety Study Comparing Japanese and Caucasian Volunteers Completed***

**SOUTH SAN FRANCISCO, CA, October 27, 2014** - Cytokinetics, Incorporated (Nasdaq: CYTK) provided an update today relating to *omecamtiv mecarbil*, the company's lead drug candidate from its cardiac muscle contractility program. The company announced that COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure) has enrolled over 275 patients towards the objective of 450 patients in the ongoing expansion phase of the trial. In addition, over 70 patients have completed the 20 weeks of dosing in the expansion phase of COSMIC-HF. Recently, the Data Monitoring Committee reviewed data from COSMIC-HF and recommended that the trial continue without any changes to the protocol. Patient enrollment in COSMIC-HF is expected to conclude by the end of 2014.

The company also announced that CY 1211, a Phase I study comparing the tolerability and pharmacokinetics of *omecamtiv mecarbil* between Japanese and Caucasian healthy volunteers, is complete and indicates no clinically meaningful differences between the two groups studied. Data from CY 1211 are expected to inform plans for the development of *omecamtiv mecarbil* in Japan and the inclusion of Japan in potential global Phase III program activities.

Amgen holds an exclusive, worldwide license to *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization rights. Additional information on COSMIC-HF and other completed Phase II clinical trials of *omecamtiv mecarbil* can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **COSMIC-HF: Phase II Clinical Trial of Oral Omecamtiv Mecarbil in Patients with Heart Failure**

COSMIC-HF is a double-blind, randomized, placebo-controlled, multicenter, dose escalation study designed to assess the pharmacokinetics 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 formulation for further evaluation. During the dose escalation phase, approximately 40 patients were randomized 1:1:1:1 to placebo or one of three different oral formulations of *omecamtiv mecarbil* in each of two ascending dose escalation cohorts to enable selection of one of these oral formulations for the expansion phase of the trial. The dose of *omecamtiv mecarbil* was 25 mg twice daily in the first dose escalation cohort and 50 mg twice daily in the second dose escalation cohort. The dose escalation phase of COSMIC-HF completed in 2013 and informed progression to the expansion phase. The ongoing expansion phase of the trial is expected to enroll approximately 450 patients randomized 1:1:1 to receive placebo, 25 mg, or 50 mg twice daily of *omecamtiv mecarbil*. Escalation to the 50 mg dose depends on the plasma concentration of *omecamtiv mecarbil* following 2 weeks of dosing with 25 mg twice daily. The primary objective of the expansion phase of COSMIC-HF is to characterize the safety, tolerability, and pharmacokinetics of oral *omecamtiv mecarbil* during 20 weeks of treatment. Secondary objectives are to assess 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) during 20 weeks of treatment. COSMIC-HF is being conducted by Amgen in collaboration with Cytokinetics.

### **CY 1211: Phase I Clinical Trial of Oral Omecamtiv Mecarbil in Japanese and Caucasian Volunteers**

CY 1211 was a Phase I single center, placebo-controlled, double-blind study comparing the pharmacokinetics of *omecamtiv mecarbil* between healthy Japanese and Caucasian volunteers. In a three-period crossover design, 36 subjects (18 Japanese and 18 Caucasians) received 3 separate treatments with at least a 7-day washout between each dosing period. Volunteers received in succession an intravenous infusion of *omecamtiv mecarbil* or placebo, multiple 25 mg doses of a modified-release oral formulation of *omecamtiv mecarbil* or placebo over 7 days, and a single 50 mg dose of a modified-release oral formulation of *omecamtiv mecarbil* or placebo. There were no clinically meaningful differences observed in the pharmacokinetics of *omecamtiv mecarbil* between Japanese and Caucasian healthy volunteers and all doses of *omecamtiv mecarbil* in CY 1211 were well tolerated. CY 1211 was conducted by Cytokinetics in collaboration with Amgen.

### **About Omecamtiv Mecarbil**

*Omecamtiv mecarbil* is a novel cardiac myosin activator and is the subject of a collaboration between Cytokinetics and Amgen. 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, which is the fundamental unit of muscle contraction in the heart. Cardiac myosin activators have been shown preclinically to work in the absence of changes in intracellular calcium in cardiac myocytes by a novel mechanism that directly stimulates the activity of the cardiac myosin motor protein. Cardiac myosin activators appear to accelerate the rate-limiting step of the myosin enzymatic cycle and shift the enzymatic cycle in favor of the force-producing state. Preclinical research has shown that this mechanism does not increase the velocity of cardiac contraction, but instead, increases the systolic ejection time, resulting in an increase in cardiac contractility and cardiac function in a potentially more oxygen-efficient manner.

### **About Heart Failure**

Heart failure is a debilitating syndrome affecting over 5 million people in the United States. Over 3 million patients are hospitalized each year with a primary or secondary diagnosis of heart failure in the United States. Heart failure is among the most common causes of hospitalization in patients over 65 years of age and is the leading cause of rehospitalization in Medicare beneficiaries. Despite available therapies, readmission rates for patients remain high within one year of hospital discharge and mortality rates exceed 50% over the five-year period following a diagnosis of heart failure. The prevalence of heart failure is increasing with the aging population and the increased likelihood of survival following acute myocardial infarction. The limited effectiveness of current therapies points to the urgent need for next-generation therapeutics.

### **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 to develop and commercialize *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. Cytokinetics is independently developing *tirasemtiv*, a fast skeletal muscle activator, as a potential treatment for diseases and medical conditions associated with neuromuscular dysfunction. *Tirasemtiv* is 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 (ALS). Cytokinetics is collaborating with Astellas Pharma Inc. to develop CK-2127107, a skeletal muscle activator structurally distinct from *tirasemtiv*, for non-neuromuscular indications. 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](http://www.cytokinetics.com).

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**Forward-Looking Statements**

*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 its partners' research and development activities, including the conduct, design, enrollment and results of clinical trials, the significance and utility of preclinical data and clinical trial results, planned interactions with regulatory authorities and the potential outcomes of such interactions; the properties and potential benefits of Cytokinetics' drug candidates, including omeclamtiv mecarbil; and the potential market for omeclamtiv mecarbil. 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, further clinical development of tirasemtiv will require significant additional funding, and Cytokinetics may be unable to obtain such additional funding on acceptable terms, if at all; 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; Astellas' and Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for CK-2127107 and omeclamtiv mecarbil, respectively; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; 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.*