Cytokinetics Announces Results from Dose Escalation Phase of COSMIC-HF Presented at Heart Failure 2017

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SOUTH SAN FRANCISCO, Calif., May 01, 2017 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK) today announced that results from the dose escalation phase of COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure), a Phase 2 trial evaluating *omecamtiv mecarbil* in patients with chronic heart failure, were presented at Heart Failure 2017, the annual congress of the Heart Failure Association of the European Society of Cardiology, held in Paris, April 29-May 2, 2017. The results were presented in a Rapid Fire Abstracts session by John Teerlink, M.D., professor of Clinical Medicine at the University of California San Francisco and director of Heart Failure at the San Francisco Veterans Affairs Medical Center. *Omecamtiv mecarbil*, a novel investigational cardiac myosin activator that increases cardiac contractility, is being developed by Amgen in collaboration with Cytokinetics for the potential treatment of heart failure.

"The dose escalation phase of COSMIC-HF supported the selection of the optimal formulation of *omecamtiv mecarbil* based on low peak-to-trough variability in plasma concentration, as well as the implementation of the PK-based dose titration strategy that was employed in the expansion phase of COSMIC-HF recently published in *The Lancet*," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President, Research and Development. "This same formulation is now being used in the ongoing Phase 3 cardiovascular clinical outcomes trial, GALACTIC-HF."

COSMIC-HF: Dose Escalation Phase Design and Results

COSMIC-HF was conducted in two phases, a dose escalation phase followed by the previously reported dose expansion phase. The dose escalation phase was a randomized, placebo-controlled, multicenter, sequential cohort design. The purpose of the dose escalation phase was to select an oral, modified-release formulation to advance into the dose expansion phase. Approximately 40 patients were randomized 1:1:1:1 to receive placebo or 1 of 3 oral formulations twice daily (BID) (M-F1, M-F2, and SCT-F2) for 7 days in each of two cohorts (25 mg BID Cohort 1; 50 mg BID Cohort 2).

The pharmacokinetics (PK) of the 3 formulations were characterized following the first dose and after 7 days of twice daily dosing. The PK of the three formulations were similar; however, the maximum plasma concentration (Cmax) and exposure over 12 hours (area under the curve or AUC12h) of M-F1 had the lowest coefficient of variability (CV), 23% and 21% respectively, at the 50 mg BID dose compared to the two other formulations. Additionally, the peak to trough fluctuation of this formulation was the lowest (1.14±0.12) as calculated from the ratio of the Cmax measured after dosing to the plasma concentration just prior to dosing (Cmax/Cpredose) at 50 mg BID. The terminal half-life was 24.6±8.7 h (25 mg BID) and 28.6±7.4 h (50 mg BID). Excessive concentrations of *omecamtiv mecarbil* occurred in one patient taking 50 mg of M-F1 on day 7 (Cmax = 1320 ng/mL) compared with the other subjects (n=9, Cmax: 349 to 654 ng/mL), which was associated with myocardial infarction characterized by symptoms of chest pain and an increased troponin.

Overall, the dose escalation phase and the outlier informed the selection of the MF-1 formulation that was used in the expansion phase of COSMIC-HF and the implementation of PK-guided dose titration to further optimize plasma concentrations of *omecamtiv mecarbil* in patients with heart failure.

About Heart Failure

Heart failure is a grievous condition that affects more than 23 million people worldwide, about half of whom have reduced left ventricular function. It is the leading cause of hospitalization and readmission in people age 65 and older. Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor. An estimated one in five people over the age of 40 are at risk of developing heart failure, and approximately 50 percent of people diagnosed with heart failure will die within five years of initial hospitalization.

About *Omecamtiv Mecarbil*

Omecamtiv mecarbil is a novel cardiac myosin activator. 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 myosin activators are thought 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 cardiac myosin activators increase contractility in the absence of changes in intracellular calcium in cardiac myocytes.

Omecamtiv mecarbil is being developed by Amgen in collaboration with Cytokinetics. Amgen holds an exclusive, worldwide license to *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization rights. Amgen has also entered an alliance with Servier for exclusive commercialization rights in Europe as well as the Commonwealth of Independent States, including Russia. Servier contributes funding for development and provides strategic support to the program.

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to increase muscle function and contractility. Cytokinetics' lead drug candidate is *tirasemtiv*, a fast skeletal troponin activator (FSTA). *Tirasemtiv* is the subject of VITALITY-ALS, an international Phase 3 clinical trial in patients with ALS. *Tirasemtiv* 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. Cytokinetics is preparing for the potential commercialization of *tirasemtiv* in North America and Europe and has granted an option to Astellas for development and commercialization in other countries. Cytokinetics is collaborating with Astellas to develop CK-2127107, a next-generation fast skeletal muscle activator. CK-2127107 is the subject of two ongoing Phase 2 clinical trials enrolling patients with spinal muscular atrophy and chronic obstructive pulmonary disease. Cytokinetics is collaborating with Amgen Inc. to develop *omecamtiv mecarbil*, a novel cardiac muscle activator. *Omecamtiv mecarbil* is the subject of GALACTIC-HF, an international Phase 3 clinical trial in patients with heart failure. Amgen holds an exclusive worldwide license to develop and commercialize *omecamtiv mecarbil* with a sublicense held by Servier for commercialization in Europe and certain other countries. Astellas holds an exclusive worldwide license to develop and commercialize CK-2127107. Licenses held by Amgen and Astellas are subject to Cytokinetics' specified co-development and co-commercialization rights. For additional information about Cytokinetics, visit http://www.cytokinetics.com/.

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 design, results, significance and utility of COSMIC-HF clinical trial results and the potential for success and timing for the progression of *omecamtiv mecarbil*; and the properties and potential benefits of Cytokinetics' 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 Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *omecamtiv mecarbil*; 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 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; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and Cytokinetics' actual results of operations, financial condition and liquidity, and the development of the industry in which it operates, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that Cytokinetics makes in this press release speak only as of the date of this press release. Cytokinetics assumes no obligation to update its forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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