Cytokinetics Announces Presentation of Additional Results From COSMIC-HF at ACC.19

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No Difference in Treatment Effects of Omecamtiv Mecarbil in Patients with Heart Failure Irrespective of Atrial Fibrillation

SOUTH SAN FRANCISCO, Calif., March 18, 2019 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional results from COSMIC-HF (**C**hronic **O**ral **S**tudy of **M**yosin Activation to **I**ncrease **C**ontractility in **H**eart **F**ailure), a Phase 2 trial evaluating *omecamtiv mecarbil* in patients with chronic heart failure, were presented by John Teerlink, M.D., Professor of Clinical Medicine, University of California San Francisco and Director of Heart Failure, San Francisco Veterans Affairs Medical Center, in a Moderated Poster Session at the American College of Cardiology's 68 th Annual Scientific Session (ACC.19) in New Orleans.

There were no statistically significant differences in the effects of treatment with *omecamtiv mecarbil* between subjects with and without atrial fibrillation (AF) on cardiac function, including systolic ejection time and stroke volume, as well as ventricular volumes, heart rate, and NT-proBNP in patients. Overall, the pattern of adverse events did not appear markedly different between treatment arms, regardless of the presence of AF at baseline. *Omecamtiv mecarbil*, a novel investigational cardiac myosin activator, is being developed for the potential treatment of heart failure under a collaboration between Amgen and Cytokinetics, with funding and strategic support from Servier.

"Atrial fibrillation is a common comorbidity in people with heart failure; its prevalence increases with increasing heart failure severity and affects up to forty percent of those with NYHA class IV disease," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President, Research and Development. "Twenty percent of patients in COSMIC-HF had both heart failure and atrial fibrillation and we're pleased to see that the treatment effects and safety of *omecamtiv mecarbil* in this key subgroup did not differ substantially from patients who did not have atrial fibrillation."

COSMIC-HF: Expansion Phase Design and Results

The expansion phase of COSMIC-HF evaluated the pharmacokinetics, pharmacodynamics, safety and tolerability of oral *omecamtiv mecarbil* in 448 patients with chronic heart failure and left ventricular systolic dysfunction. Patients were randomized 1:1:1 to receive either placebo or treatment with *omecamtiv mecarbil* dosed as 25 mg twice daily or 25 mg twice daily with dose escalation to 50 mg twice daily, depending on a plasma concentration of *omecamtiv mecarbil* after two weeks of treatment. The study met its primary pharmacokinetic objective and showed statistically significant improvements in all pre-specified secondary measures of cardiac function in the treatment group receiving pharmacokinetic-based (PK) dose titration.

In analyses announced today, measures of efficacy of *omecamtiv mecarbil* were compared after 20 weeks of treatment for patients with and without AF, a subgroup whose enrollment was limited to approximately 20 percent of the overall study population. Between 32 patients with AF and 117 patients without AF, there were no significant differences in the effect of *omecamtiv mecarbil* on systolic ejection time (p=.69), stroke volume (p=.38), left ventricular end-diastolic dimension (p=.90), left ventricular end-systolic dimension (p=.75), heart rate (p=.08) and NT-proBNP (p=.43). These results suggest that patients with both heart failure and AF respond similarly to treatment with *omecamtiv mecarbil* as patients with heart failure without AF.

About *Omecamtiv Mecarbil* and the Phase 3 Clinical Trials Program

Omecamtiv mecarbil is a novel, selective cardiac myosin activator that binds to the catalytic domain of myosin. Preclinical research has shown that cardiac myosin activators increase cardiac contractility without affecting intracellular myocyte calcium concentrations or myocardial oxygen consumption.[i,ii,iii] 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.

Omecamtiv mecarbil is being developed for the potential treatment of heart failure with reduced ejection fraction (HFrEF) under a collaboration between Amgen and Cytokinetics, with funding and strategic support from Servier. *Omecamtiv mecarbil* is the subject of a comprehensive Phase 3 clinical trials program comprised of GALACTIC-HF (**G**lobal **A**pproach to **L**owering **A**dverse **C**ardiac Outcomes **T**hrough **I**mproving **C**ontractility in **H**eart **F**ailure), a large, Phase 3 global cardiovascular outcomes trial being conducted by Amgen in collaboration with Cytokinetics and METEORIC-HF (**M**ulticenter **E**xercise **T**olerance **E**valuation of ***O**mecamtiv Mecarbil* **R**elated to **I**ncreased **C**ontractility in **H**eart **F**ailure), a Phase 3 clinical trial designed to evaluate the effect of treatment with *omecamtiv mecarbil* on exercise capacity, being conducted by Cytokinetics in collaboration with Amgen.

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and best-in-class muscle inhibitors 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 impact muscle function and contractility. Cytokinetics is collaborating with Amgen Inc. (Amgen) to develop *omecamtiv mecarbil*, a novel cardiac muscle activator. *Omecamtiv mecarbil* is the subject of an international clinical trials program in patients with heart failure including GALACTIC-HF and METEORIC-HF. 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. Cytokinetics is collaborating with Astellas Pharma Inc. (Astellas) to develop *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA). *Reldesemtiv* was the subject of a Phase 2 clinical study in patients with spinal muscular atrophy which showed increases in measures of endurance and stamina consistent with the mechanism of action. *Reldesemtiv* is currently the subject of a Phase 2 clinical trial in patients with amyotrophic lateral sclerosis. Astellas holds an exclusive worldwide license to develop and commercialize *reldesemtiv*. Licenses held by Amgen and Astellas are subject to specified co-development and co-commercialization rights of Cytokinetics. Cytokinetics is also developing CK-274, a novel cardiac myosin inhibitor that company scientists discovered independent of its collaborations, for the potential treatment of hypertrophic cardiomyopathies. Cytokinetics continues its over 20-year history of pioneering innovation in muscle biology and related pharmacology focused to diseases of muscle dysfunction and conditions of muscle weakness.

For additional information about Cytokinetics, visit www.cytokinetics.com and follow us on Twitter, LinkedIn, Facebook and YouTube.

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; the design, results, significance and utility of preclinical study results; 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, 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 trial 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 FDA 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' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv*; 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; 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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[i] Planelles-Herrero VJ, Hartman JJ, Robert-Paganin J. et al. Mechanistic and structural basis for activation of cardiac myosin force production by *omecamtiv mecarbil*. *Nat Commun*. 2017;8:190.

[ii] Shen YT, Malik FI, Zhao X, et al. Improvement of cardiac function by a cardiac myosin activator in conscious dogs with systolic heart failure. *Circ Heart Fail*. 2010; 3: 522-27.

[iii] Malik FI, Hartman JJ, Elias KA, Morgan BP, Rodriguez H, Brejc K, Anderson RL, Sueoka SH, Lee KH, Finer JT, Sakowicz R. Cardiac myosin activation: a potential therapeutic approach for systolic heart failure. *Science*. 2011 Mar 18;331(6023):1439-43.

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