Cytokinetics Announces Additional Results From COSMIC-HF at the American Heart Association Scientific Sessions 2017

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SOUTH SAN FRANCISCO, Calif., Nov. 13, 2017 (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 clinical trial evaluating *omecamtiv mecarbil* in patients with chronic heart failure and left ventricular systolic dysfunction, were presented by John Teerlink, M.D. in an Abstract Rapid Fire Oral presentation at the American Heart Association Scientific Sessions 2017 in Anaheim, Calif. Dr. Teerlink is Professor of Clinical Medicine at the University of California San Francisco and Director of Heart Failure at the San Francisco Veterans Affairs Medical Center. In this post-hoc responder analysis, the proportion of patients achieving various thresholds in the percent reduction of NT-proBNP were larger in patients who received *omecamtiv mecarbil* than in patients who received placebo. *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.

"NT-proBNP is a biomarker of ventricular wall stress, with higher levels reflecting more severe heart failure," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President of Research & Development. "This analysis showed that *omecamtiv mecarbil* reduces NT-proBNP in a potentially meaningful way, consistent with a reduction in ventricular wall stress. With these positive changes observed for NT-proBNP and other measures relevant to heart failure in COSMIC-HF, we now look forward in GALACTIC-HF to learning if *omecamtiv mecarbil* can improve clinical outcomes in patients with heart failure."

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 trial 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.

This post-hoc responder analysis evaluated percent changes in NT-proBNP between patients receiving placebo or *omecamtiv mecarbil* from baseline to week 20 in the PK titration group of COSMIC-HF. Responders were defined as those patients who achieved various thresholds in the percent reduction of NT-proBNP from baseline to 20 weeks. The percentage of patients receiving *omecamtiv mecarbil* and meeting each responder definition was compared to the corresponding percentage of patients in the placebo group meeting the same responder definition. In patients receiving *omecamtiv mecarbil* compared to placebo, there was a statistically significant greater proportion of responders at each threshold except for that evaluating a > 50 percent decrease from baseline.

Percent decrease in NT-proBNP from baseline to 20 weeks	Proportion of Responders		
	Omecamtiv Mecarbil	Placebo	p value
> 20%	48%	36%	0.047
> 30%	42%	30%	0.047
> 40%	33%	21%	0.039
> 50%	20%	15%	>0.05

The data from this post-hoc analysis suggest *omecamtiv mecarbil* reduced myocardial wall stress, perhaps providing a mechanism for beneficial ventricular reverse remodeling, which is a reversal of the ventricular enlargement that occurs in patients with systolic heart failure, that may translate into clinically meaningful effects on cardiovascular outcomes.

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 in the United States. Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor. In the United States, 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 muscle 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 (FDA) and orphan medicinal product designation by the European Medicines Agency for the potential treatment of ALS. Cytokinetics is preparing for the potential commercialization of *tirasemtiv* in North America and Europe and has granted an option to Astellas Pharma Inc. (“Astellas”) for development and commercialization in other countries. Cytokinetics is collaborating with Astellas to develop CK-2127107, a next-generation FSTA. CK-2127107 has been granted orphan drug designation by the FDA for the potential treatment of SMA. CK-2127107 is the subject of three ongoing Phase 2 clinical trials enrolling patients with spinal muscular atrophy, chronic obstructive pulmonary disease and ALS. Astellas is also conducting a Phase 1b clinical trial of CK-2127107 in elderly adults with limited mobility. Cytokinetics is collaborating with Amgen Inc. (“Amgen”) to develop *omecamtiv mecarbil*, a novel cardiac myosin 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, the properties and potential benefits of Cytokinetics’ drug candidates, including *omecamtiv mecarbil*; the design, timing, results and significance of GALACTIC-HF, the Phase 3 clinical trial of *omecamtiv mecarbil* in subjects with chronic heart failure and reduced ejection fraction; and the potential for eventual regulatory approval, commercialization and launch of Cytokinetics’ product 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 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; 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.

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