Cytokinetics Announces Presentation of Additional Results From COSMIC-HF at Heart Failure 2016 Congress

May 23, 2016 11:30 AM EDT

Treatment with Omecamtiv Mecarbil Produced Progressive and Sustained Effects On Cardiac Function as Measured by Reductions in Diastolic Ventricular Volume and NT-proBNP

SOUTH SAN FRANCISCO, Calif., May 23, 2016 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK) today announced that additional results from COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure), a Phase 2b trial evaluating *omecamtiv mecarbil* in patients with chronic heart failure, were presented in a poster titled "COSMIC-HF: Improved Contractility and Evolution of Ventricular Remodeling through Time" at Heart Failure 2016, the annual congress of the Heart Failure Association of the European Society of Cardiology, in Florence, Italy. The results presented showed that *omecamtiv mecarbil* improved left ventricular (LV) systolic function, LV end-diastolic volume and NT-proBNP over time, suggesting potentially favorable ventricular remodeling and progressive reduction in myocardial wall stress. *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.

"For the first time, we have evidence that increasing cardiac contractility by chronic treatment with *omecamtiv mecarbil* may result in a progressive reduction in ventricular size," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President, Research and Development. "We are preparing for a potential Phase 3 program in collaboration with Amgen in which we would learn if these effects on cardiac function are durable over longer periods of treatment and may also translate to improved cardiovascular outcomes."

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 placebo, to *omecamtiv mecarbil* 25 mg twice daily, or to a dose titration group in which an initial dose of 25 mg twice daily could be increased to 50 mg twice daily depending on the plasma concentration of *omecamtiv mecarbil* after two weeks of treatment with the 25 mg twice daily dose. Data from the expansion phase were presented as a Late-Breaking Clinical Trial at the American Heart Association's Scientific Sessions in November, 2015 and showed that this dose titration strategy maintained concentrations of *omecamtiv mecarbil* within a range associated with potentially beneficial pharmacodynamic effects avoiding excessive concentrations.

Placebo-corrected data from the dose titration group are shown in the table below. Increases in systolic ejection time (SET) and stroke volume, and decreases in LV end-systolic volume, were similar after both 12 and 20 weeks of treatment with *omecamtiv mecarbil*; however, LV end-diastolic volume decreased progressively from 12 to 20 weeks, with the decrease after 20 weeks nearly twice that observed after 12 weeks. NT-proBNP (a biomarker that is elevated in heart failure, with higher elevations reflecting more severe heart failure) also fell progressively over time and, of particular note, had declined even further four weeks after treatment discontinuation (-1306 ± 376 pg/mL; p=0.0006). Heart rate also declined significantly after 2, 12 and 20 weeks of treatment ranging from 2-4 beats per minute and returning nearly to baseline four weeks after treatment discontinuation (-1.2±1.2 beats/min: p = 0.29).

Endpoint	Baseline*	Changes from Baseline* *(p value for change on omecamtiv mecarbil vs. placebo)*		
		2 Weeks	12 weeks	20 weeks
Systolic Ejection Time (msec)	**298 ± 333**	**Not measured**	**22 ± 3** ***(p < 0.0001)***	**25 ± 3** ***(p < 0.0001)***
Stroke Volume (mL)	**52.4 ± 14.9**		**3.2 ± 1.6** ***(p = 0.038)***	**3.6 ± 1.6** ***(p = 0.022)***
LV end-systolic volume (mL)	**157.1 ± 77.7**		**-9.9 ± 3.8** ***(p = 0.009)***	**-11.2 ± 3.9** ***(p = 0.005)***
LV end-diastolic volume (mL)	**215.9 ± 88.8**		**-5.8 ± 4.2** ***(p = 0.17)***	**-10.7 ± 4.6** ***(p = 0.021)***
NT-proBNP (pg/mL) ***(Baseline is median [Q1, Q3])***	**1719** ***[881, 3060]***	**-302 ± 204** ***(p = 0.14)***	**-623 ± 364** ***(p = 0.087)***	**-970 ± 357** ***(p = 0.007)***
Heart rate (beats/min)	**70 ± 12**	**-2.2 ± 0.8** ***(p = 0.007)***	**-4.0 ± 1.0** ***(p < 0.0001)***	**-3.0 ± 1.1** ***(p = 0.007)***
*mean ± SD unless otherwise noted				

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. Les Laboratoires Servier obtained an exclusive option to commercialize *omecamtiv mecarbil* in Europe.

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, for the potential treatment of 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 for the potential treatment of ALS. Cytokinetics retains the right to develop and commercialize *tirasemtiv*. Cytokinetics is collaborating with Amgen Inc. to develop *omecamtiv mecarbil*, a novel cardiac muscle activator, for the potential treatment of heart failure. Cytokinetics is collaborating with Astellas Pharma Inc. to develop CK-2127107, a fast skeletal muscle activator, for the potential treatment of spinal muscular atrophy and chronic obstructive pulmonary disease. Amgen holds an exclusive license worldwide to develop and commercialize *omecamtiv mecarbil* and Astellas holds an exclusive license worldwide to develop and commercialize CK-2127107. Both licenses are subject to Cytokinetics' specified development and commercialization participation 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*; plans and timing of the ongoing Phase 2 clinical trial of *omecamtiv mecarbil* and a potential Phase 3 clinical trial of *omecamtiv mecarbil*; 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, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; and 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. 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.

Contact:
Cytokinetics
Diane Weiser
Vice President, Corporate Communications, Investor Relations
(415) 290-7757

Cytokinetics, Inc