Cytokinetics Announces Results From METEORIC-HF and Additional Data From GALACTIC-HF Presented at the American College of Cardiology 71st Annual Scientific Session

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No Effect of Omecamtiv Mecarbil On Exercise Capacity
in Patients with Heart Failure with Reduced Ejection Fraction in METEORIC-HF

Healthcare Resource Utilization and Cost Analysis from GALACTIC-HF Demonstrate Treatment with Omecamtiv Mecarbil Led to 19% Cost Reduction Per Patient in Key Subgroup

Additional Results from GALACTIC-HF Indicate Treatment with Omecamtiv Mecarbil
Associated with Similar Risk Reduction in Both Hospitalized Patients and Outpatients

SOUTH SAN FRANCISCO, Calif., April 03, 2022 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the full results from 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 of *omecamtiv mecarbil* in patients with heart failure with reduced ejection fraction (HFrEF), were presented by Michael Felker, M.D., Professor of Medicine, Duke Clinical Research Institute, at the American College of Cardiology 71st Annual Scientific Session (ACC.22). Additional data from 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) were also presented including a healthcare resource utilization analysis and an analysis of the effect of treatment with *omecamtiv mecarbil* in hospitalized patients compared to outpatients.

METEORIC-HF: No Effect of Treatment with *Omecamtiv Mecarbil* on Exercise Capacity

METEORIC-HF evaluated the effect of treatment with *omecamtiv mecarbil* compared to placebo on exercise capacity as determined by cardiopulmonary exercise testing (CPET) following 20 weeks of treatment in patients with HFrEF receiving standard of care therapy. The trial enrolled 276 patients in 9 countries. At baseline, patients had an average left ventricular ejection fraction (LVEF) of 27% and an average peak oxygen uptake (pVO_2) of 14.7 ml/kg/min; 79% were New York Heart Association (NYHA) Functional Class II. After 20 weeks of treatment, there was no change in pVO_2 in patients treated with *omecamtiv mecarbil* versus placebo. Patients treated with *omecamtiv mecarbil* had an average change from baseline in pVO_2 of -0.2 ml/kg/min compared to 0.2 ml/kg/min for patients on placebo (p=0.13). There was no beneficial effect observed in any of the secondary endpoints, including change in total workload during exercise, change in ventilatory efficiency and change in daily physical activity. Adverse events, including major cardiac events, were similar between the treatment arms, even with patients reaching peak exercise.

GALACTIC-HF: Treatment with *Omecamtiv Mecarbil* Led to 19% Cost Reduction Per Patient Among Patient Subgroup with Ejection Fraction Less than 30%, Without Atrial Fibrillation and Digoxin

Nihar R. Desai, M.D., MPH, Associate Professor of Medicine, Associate Chief, Cardiovascular Medicine, Yale School of Medicine, Center for Outcomes Research and Evaluation, presented new data on the healthcare resource use, intensity and costs among patients treated with *omecamtiv mecarbil* in GALACTIC-HF. In this analysis, a subgroup of 5,369 patients (65%) of the 8,256 patients enrolled in GALACTIC-HF met the specific criteria selected. The excluded patient subgroup comprised those who had atrial fibrillation and were taking digoxin or had an ejection fraction (EF) >30%. In the selected subgroup, *omecamtiv mecarbil* was associated with significant reductions in risk of a first heart failure event (relative risk reduction (RRR) 15%, absolute risk reduction (ARR) 3.8, number needed to treat (NNT) 26.2), total HF events (RRR 17%, ARR 6.8, NNT 14.7), and cumulative heart failure events. In this selected subgroup of 5,369 patients, treatment with *omecamtiv mecarbil* also significantly reduced resource intensity, measured by total days in hospital among patients being hospitalized (rate ratio 0.90, 95% CI 0.82–0.99). The estimated potential cost reductions within the selected subgroup related to heart failure events were $3,085, a 19% reduction per patient. Of the cost reductions, 99% were due to heart failure hospitalizations avoided by those patients in GALACTIC-HF who were treated with *omecamtiv mecarbil*.

GALACTIC-HF: Treatment with *Omecamtiv Mecarbil* Associated with Similar Risk Reduction in the Primary Composite Endpoint in Both Hospitalized Patients and Outpatients

Kieran F. Docherty, M.D., Clinical Lecturer, Institute of Cardiovascular and Medical Sciences, University of Glasgow presented additional data from GALACTIC-HF on the effect of *omecamtiv mecarbil* in hospitalized patients compared with outpatients. GALACTIC-HF was designed to enroll 25% of patients during hospitalization for worsening heart failure. Of 8,232 patients enrolled, 2,084 (25%) were hospitalized at the time of randomization, while 6,148 (75%) were randomized as outpatients. At baseline, compared with outpatients, hospitalized patients had higher NYHA Functional Class, were more likely to have atrial fibrillation, had lower systolic blood pressure, and had higher resting heart rate, more severe renal impairment, and higher NT-proBNP.

The rate of the primary outcome was higher in hospitalized patients in the placebo group (38.3/100 person-years [PY]) than in outpatients (23.1/100 PY) with an adjusted hazard ratio (HR) of 1.21 (95% CI 1.12, 1.31). There was a stepwise gradient in risk, with those randomized as outpatients in the placebo group within 3 months of a heart failure event at the highest risk (26.6/100 patient years (PY)) as compared with those 9-12 months post-event (19.0/100 PY) with an adjusted hazard ratio (HR) of 1.20 (95% CI 1.01, 1.42), p for trend = 0.008). The effect of *omecamtiv mecarbil* versus placebo on the primary outcome was similar in hospitalized patients (HR 0.89, 95% CI 0.78, 1.01) and outpatients (HR 0.94, 95% CI 0.86, 1.02), indicating that *omecamtiv mecarbil* similarly reduced the risk of the primary outcome both when initiated in hospitalized patients and in outpatients. In both hospitalized patients and outpatients, the initiation of *omecamtiv mecarbil* was safe and well tolerated. Treatment-emergent serious adverse events occurred more frequently in patients randomized during hospitalization but did not differ significantly between the treatment groups.

"The results of METEORIC-HF continue to emphasize the difficulty of improving exercise capacity in patients with heart failure and reduced ejection fraction even as strides are made to improve clinical outcomes in these same patients. While there was no effect of *omecamtiv mecarbil* on exercise capacity in METEORIC-HF, we are encouraged that the results further reinforce the overall safety profile of *omecamtiv mecarbil* observed in GALACTIC-HF," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "New and additional data from GALACTIC-HF continue to elaborate on our novel cardiac myosin activator including its impact on healthcare resource utilization and its use in both hospital and outpatient settings. These findings further our understanding of the potential benefit *omecamtiv mecarbil* may have in patients at risk for

worsening heart failure, as well as the impact it may have on potential cost savings for the healthcare system."

About *Omecamtiv Mecarbil*

Omecamtiv mecarbil is an investigational, selective, small molecule cardiac myosin activator, the first of a novel class of myotropes[1] designed to directly target the contractile mechanisms of the heart, binding to and recruiting more cardiac myosin heads to interact with actin during systole. *Omecamtiv mecarbil* was designed to increase the number of active actin-myosin cross bridges during each cardiac cycle and consequently augment the impaired contractility that is associated with heart failure with reduced ejection fraction (HFrEF). Preclinical research has shown that *omecamtiv mecarbil* increases cardiac contractility without increasing intracellular myocyte calcium concentrations or myocardial oxygen consumption.[2-4]

The development program for *omecamtiv mecarbil* is assessing its potential for the treatment of HFrEF. Positive results from GALACTIC-HF, the first Phase 3 clinical trial of *omecamtiv mecarbil* demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of cardiovascular (CV) death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure) compared to placebo in patients treated with standard of care. No reduction in the secondary endpoint of time to CV death was observed. Adverse events and treatment discontinuation of study drug were balanced between treatment arms. The FDA has accepted for filing the NDA for *omecamtiv mecarbil* based on the results from GALACTIC-HF and has assigned a Prescription Drug User Fee Act (PDUFA) date of November 30, 2022.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide[1] about half of whom have reduced left ventricular function.[2,3] It is the leading cause of hospitalization and readmission in people age 65 and older.[4,5] Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.[6] 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.[7,8] More than 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have severe heart failure.[9]

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and next-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised. 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 readying for the potential commercialization of *omecamtiv mecarbil*, its cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is also developing *aficamten*, a next-generation cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is also being evaluated in non-obstructive HCM in Cohort 4 of the Phase 2 clinical trial, REDWOOD-HCM. Cytokinetics is also developing *reldesemtiv*, an investigational fast skeletal muscle troponin activator, currently the subject of COURAGE-ALS, a Phase 3 clinical trial in patients with amyotrophic lateral sclerosis (ALS). 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 the potential treatment effects, cost savings or other potential benefits of *omecamtiv mecarbil* to patients with heart failure and the likelihood of FDA approval of *omecamtiv mecarbil*, if ever, by the target PDFUFA date of November 30, 2022. 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; Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy; the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; 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.

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Source: Cytokinetics, Incorporated