Cytokinetics Announces Completion of Enrollment in METEORIC-HF, The Second Phase 3 Clinical Trial of Omecamtiv Mecarbil in Patients With Heart Failure With Reduced Ejection Fraction

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Top Line Results of METEORIC-HF Expected in Early 2022

Company Plans to Submit NDA in 2H 2021 Based on Positive Results of GALACTIC-HF

SOUTH SAN FRANCISCO, Calif., June 15, 2021 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced the completion of patient enrollment in 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), the second Phase 3 clinical trial of *omecamtiv mecarbil*. METEORIC-HF is designed to evaluate the effect of treatment with *omecamtiv mecarbil* compared to placebo on exercise capacity as determined by cardiopulmonary exercise testing (CPET) in patients with heart failure with reduced ejection fraction (HFrEF).

"We would like to thank the investigators and clinical site coordinators for their commitment to METEORIC-HF, particularly given the challenges they overcame enrolling a trial in the midst of a global pandemic," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "Based on recent interactions with FDA, we plan to submit the New Drug Application for *omecamtiv mecarbil* this year based on results from GALACTIC-HF. Results from METEORIC-HF are expected in early 2022 and may further elaborate on potential effects in patients with severe heart failure."

"Exercise intolerance is a common symptom among people suffering from heart failure with reduced ejection fraction and can seriously limit quality of life," said Gregory Lewis, M.D., Heart Failure Section Head and Director, Cardiopulmonary Exercise Testing Laboratory, Massachusetts General Hospital. "We look forward to assessing whether improvement in cardiac contractility by a novel mechanism cardiac myosin activator may increase exercise capacity and potentially lead to greater mobility and function for patients living with HFrEF."

About METEORIC-HF

METEORIC-HF opened to enrollment in early 2019 and was designed to enroll 270 patients with HFrEF at sites throughout the U.S., Canada and Europe to evaluate the effect of treatment with *omecamtiv mecarbil* compared to placebo on exercise capacity as determined by CPET. Patients are required to have a left ventricular ejection fraction (LVEF) ≤35 percent, New York Heart Association (NYHA) heart failure class II or III and reduced exercise capacity compared to age matched controls. Patients were randomized in a 2:1 fashion to *omecamtiv mecarbil*, starting at 25 mg twice daily and titrated to 25, 37.5 or 50 mg twice daily based on the same PK-guided dosing regimen as used in GALACTIC-HF, the Phase 3 cardiovascular outcomes trial of *omecamtiv mecarbil*, or to placebo. The primary endpoint is the change in peak oxygen uptake (pVO2) on CPET from baseline to Week 20. Secondary endpoints include the change in total workload during CPET from baseline to Week 20 and the change in the average daily activity units measured over a 2-week period from baseline (Week -2 to Day 1) to Week 18-20 as determined using accelerometry.

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

Omecamtiv mecarbil is an investigational selective 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. Preclinical research has shown that *omecamtiv mecarbil* increases cardiac contractility without increasing intracellular myocyte calcium concentrations or myocardial oxygen consumption.[2-4] 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 HFrEF and is the subject of a comprehensive Phase 3 clinical trials program composed of GALACTIC-HF and METEORIC-HF. The results from GALACTIC-HF, published in the *New England Journal of Medicine,* demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of time to first heart failure event (heart failure hospitalization and other urgent treatment for heart failure) or cardiovascular (CV) death compared to placebo in patients treated with standard of care (hazard ratio, 0.92; 95% confidence interval [CI] 0.86, 0.99; p=0.025). No reduction in the secondary endpoint of time to CV death was observed in the overall population.[5] Supplemental analyses indicated a greater treatment effect in patients with a lower LVEF (LVEF ≤28%, n=4,456, hazard ratio, 0.84; 95% CI 0.77, 0.92; interaction p=0.003). Effects in GALACTIC-HF were observed without evidence of an increase in the overall rates of myocardial ischemic events, ventricular arrhythmias or death from cardiovascular or all causes.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide[6] about half of whom have reduced left ventricular function.[7,8] It is the leading cause of hospitalization and readmission in people age 65 and older.[9,10] Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.[11] 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 are expected to die within five years of initial hospitalization.[12,13] More than 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have severe heart failure.[14]

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 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 preparing a U.S. NDA submission of *omecamtiv mecarbil*, its novel cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is conducting METEORIC-HF, a second Phase 3 clinical trial of *omecamtiv mecarbil*. Cytokinetics is also developing CK-274, a next-generation cardiac myosin inhibitor, for the potential treatment of hypertrophic cardiomyopathies (HCM). Cytokinetics is conducting REDWOOD-HCM, a Phase 2 clinical

trial of CK-274 in patients with obstructive HCM. Cytokinetics is also developing *reldesemtiv*, a fast skeletal muscle troponin activator for the potential treatment of ALS and other neuromuscular indications following conduct of FORTITUDE-ALS and other Phase 2 clinical trials. The company is preparing for the potential advancement of CK-274 to a Phase 3 clinical trial in obstructive HCM and *reldesemtiv* to a Phase 3 clinical trial in 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, the potential benefits of *omecamtiv mecarbil*, including its ability to represent a novel therapeutic strategy to increase cardiac muscle function and restore cardiac performance; the timing and likelihood of any regulatory submissions or approval of *omecamtiv mecarbil*, the availability of topline results from METEORIC-HF in early 2022, Cytokinetics' research and development activities, the design, timing, results, significance and utility of preclinical and clinical results; and the properties and potential benefits of Cytokinetics' other 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; 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.

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

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Source: Cytokinetics, Incorporated