



Cytokinetics Announces Additional Results From GALACTIC-HF Presented at the 17th Global Cardiovascular Clinical Trialists

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Supplemental Analyses of Primary Composite Endpoint Further Demonstrate Effect of Omecamtiv Mecarbil In Patients with Lower Ejection Fraction

SOUTH SAN FRANCISCO, Calif., Dec. 07, 2020 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional results from GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), the Phase 3 event-driven cardiovascular outcomes clinical trial of *omecamtiv mecarbil*, were presented by John Teerlink, M.D., Professor of Medicine, University of California San Francisco, Director of Heart Failure, San Francisco Veterans Affairs Medical Center and Executive Committee Chair, GALACTIC-HF, at the 17th Global Cardiovascular Clinical Trialists Forum (CVCT).

"These results shed light on advanced heart failure patients who may benefit more from potential treatment with *omecamtiv mecarbil*," said John Teerlink, M.D. "These sicker patients continue to have substantial persistent risk despite receiving standard of care therapy and, based on the progressive nature of their disease, are frequently unable to tolerate guideline-directed medical therapy as their disease worsens. These additional data from GALACTIC-HF suggest that *omecamtiv mecarbil* may provide a new treatment option for this critical population of patients."

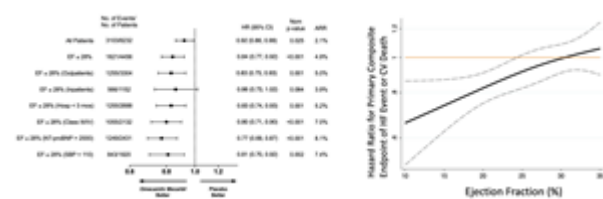
GALACTIC-HF: Supplemental Analyses

GALACTIC-HF enrolled 8,256 patients who were at risk of hospitalization and death, despite being well treated on standard of care therapy. As previously reported, after a median duration of follow-up of 21.8 months, the trial demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of heart failure events (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 population¹.

The effect of *omecamtiv mecarbil* on the primary composite endpoint in GALACTIC-HF was consistent across most prespecified subgroups and with a potentially greater treatment effect suggested in patients with a lower left ventricular ejection fraction (LVEF $\leq 28\%$, $n=4,456$, hazard ratio, 0.84; 95% CI 0.77, 0.92; interaction $p=0.003$). Supplemental analyses of this lower ejection fraction subgroup in GALACTIC-HF presented at CVCT showed that this potentially greater treatment effect in patients who received *omecamtiv mecarbil* was consistently observed in patients with characteristics that may indicate advanced heart failure status, such as being hospitalized within the last 3 months (HR 0.83, 95% CI 0.74 – 0.93, $p=0.001$), having New York Association Class III or IV heart failure (HR 0.80, 95% CI 0.71 – 0.90, $p<0.001$), higher N-terminal-pro brain natriuretic peptide levels (HR 0.77, 95% CI 0.69 – 0.87, $p<0.001$), and lower blood pressures (HR 0.81, 95% CI 0.70 – 0.92, $p=0.002$). The absolute risk reductions (ARR) ranged from 5.2% to 8.1% in these subgroups as compared to the ARR of 2.1% observed in the overall population.

Additionally, a supplemental analysis of the continuous relationship between ejection fraction and the hazard ratio for the primary composite endpoint in GALACTIC-HF suggested a potentially stronger treatment effect of *omecamtiv mecarbil* in patients with increasingly lower ejection fractions.

Supplemental Analyses of GALACTIC-HF



Left: Forest plot of the primary composite endpoint for subgroups of patients with lower left ventricular ejection fraction (LVEF) and other markers of heart failure status. Right: Hazard ratio for the primary composite endpoint of HF event or CV death as a function of ejection fraction.

"These new data from GALACTIC-HF reinforce the relationship between the primary pharmacologic effect of *omecamtiv mecarbil* to improve cardiac systolic function and its impact on heart failure outcomes, as it stands to reason that those with more impaired function may benefit most from this novel mechanism therapy," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "We look forward to sharing additional analyses in upcoming publications and presentations which will elaborate further on these and other ongoing analyses of data arising from GALACTIC-HF."

GALACTIC-HF: Trial Design And Primary Results

GALACTIC-HF² (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), one of the largest Phase 3 global cardiovascular outcomes studies in heart failure ever conducted, enrolled 8,256 patients in 35 countries across 945 sites with HFrEF, New York Heart Association (NYHA) class II-IV, left ventricular ejection fraction (LVEF) $\leq 35\%$, elevated natriuretic peptides and either current hospitalization for heart failure or history of hospitalization or emergency department visit for heart failure within a year. Patients were randomized to either oral

placebo or a starting dose of 25 mg *omecamtiv mecarbil* twice daily (maintenance dose of 50 mg, 37.5 mg, or 25 mg twice daily) guided by pharmacokinetic-guided dose selection. A blood test, the QMS *Omeclamtiv Mecarbil* Immunoassay (the OM Test) was used to measure plasma levels of *omecamtiv mecarbil* in each patient in order to guide selection of the appropriate maintenance dose.

The primary composite endpoint of this double-blind, placebo-controlled, event-driven trial was time to CV death or first heart failure event (heart failure hospitalization and other urgent treatment for heart failure). Secondary endpoints were: time to CV death, patient reported outcomes (measured by Kansas City Cardiomyopathy Questionnaire [KCCQ] Total Symptom Score [TSS]), time to first heart failure hospitalization and time to all-cause death. A first primary endpoint event occurred in 1,523 of 4,120 patients (37.0%) in the *omecamtiv mecarbil* group and in 1,607 of 4,112 patients (39.1%) in the placebo group (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. The effect on the primary endpoint was observed without evidence of an increase in the overall rates of myocardial ischemic events, ventricular arrhythmias or death from cardiovascular or all causes.

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

Omeclamtiv mecarbil is an investigational selective cardiac myosin activator, the first of a novel class of myotropes³ 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.⁴⁻⁶ 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.

Omeclamtiv mecarbil is being developed for the potential treatment of heart failure with reduced ejection fraction (HFrEF) and is the subject of a comprehensive Phase 3 clinical trials program composed of GALACTIC-HF and METEORIC-HF (Multicenter Exercise Tolerance Evaluation of *Omeclamtiv Mecarbil* Related to Increased Contractility in Heart Failure), a Phase 3 clinical trial designed to evaluate the effect of treatment with *omecamtiv mecarbil* compared to placebo on exercise capacity.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide⁷ about half of whom have reduced left ventricular function.^{8,9} It is the leading cause of hospitalization and readmission in people age 65 and older.^{10, 11} Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.¹² 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.^{13,14}

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 for regulatory interactions for *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 considering potential advancement of *reldesemtiv* to Phase 3 pending ongoing regulatory interactions. 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 GALACTIC-HF clinical trial; statements relating to the METEORIC-HF clinical trial; 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 potential approval of *omecamtiv mecarbil* by the FDA or any other regulatory authority and the timing of such approvals; Cytokinetics' and its partners' 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' 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; 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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Source: Cytokinetics, Incorporated