Cytokinetics Announces Data From REDWOOD-HCM OLE and GALACTIC-HF Presented as Late Breaking Science Presentations at the European Society of Cardiology Heart Failure 2022 Congress

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Data from Up to Six Months of Treatment with Aficamten Show Significant and Sustained Reductions in LVOT Gradients with Improvements in Functional Class, Symptoms, and Biomarkers

Analyses from GALACTIC-HF Show Patients with Low Blood Pressure Have Increased Treatment Effect

SOUTH SAN FRANCISCO, Calif., May 23, 2022 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced positive data relating to *aficamten* from REDWOOD-HCM OLE (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM O**pen **L**abel **E**xtension) and the results from two additional analyses of *omecamtiv mecarbil* 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), all presented in Late-Breaking Science Sessions at Heart Failure 2022, an International Congress of the European Society of Cardiology. The analysis from GALACTIC-HF related to low blood pressure has been simultaneously published in the *European Heart Journal*.

"This first analysis from REDWOOD-HCM OLE showed that ongoing treatment with *aficamten*, now out to 6 months, resulted in sustained and substantial reductions in LVOT gradients, as well as improvements in functional class and symptoms. Overall safety and tolerability remain favorable, and all patients enrolled remain on *aficamten.* We look forward to sharing additional longer-term data later this year," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "In addition, the analysis of patients from GALACTIC-HF with lower blood pressure, often very challenging to treat, showed that the treatment effect of *omecamtiv mecarbil* was greater than in the overall population, blood pressure was not adversely affected, and safety was similar to placebo in these patients. In another analysis, the treatment effect of *omecamtiv mecarbil* was also comparable in patients with or without tricuspid regurgitation. These findings add to the growing body of evidence demonstrating that patients with clinical features suggestive of high-risk heart failure respond favorably to *omecamtiv mecarbil*."

REDWOOD-HCM OLE: First Long-Term Data from Open Label Extension

Ahmad Masri, M.D., Assistant Professor of Medicine, Division of Cardiovascular Medicine, School of Medicine, Oregon Health & Science University, presented the first long-term data from REDWOOD-HCM OLE. Patients enrolled in REDWOOD-HCM OLE have completed participation in REDWOOD-HCM, the Phase 2 clinical trial of *aficamten*. The primary endpoint is the incidence of adverse events and left ventricular ejection fraction (LVEF) <50%. Secondary endpoints include measures of the long-term effects of *aficamten* on left ventricular outflow tract gradient (LVOT-G), and assessments of steady state pharmacokinetics. The trial also includes a cardiac magnetic resonance imaging sub-study to assess changes in cardiac morphology, function and fibrosis. All enrolled patients receive *aficamten*. After entry into REDWOOD-HCM OLE, each patient started at 5 mg once daily and underwent echocardiography-guided dose titration approximately every two weeks during the first six weeks and subsequently will continue to have study visits approximately every twelve weeks thereafter.

Data from 38 patients enrolled in REDWOOD-HCM OLE were presented today, including 30 patients treated for 12 weeks and 19 patients treated for 24 weeks. The data showed that treatment with *aficamten* was associated with substantial reductions in the average resting LVOT-G (mean change from baseline (SD) = -32.6 (28) mmHg, p<0.0001 at 12 weeks, -32.8 (32.3) mmHg, p=0.0003 at 24 weeks) and Valsalva LVOT-G (-42.7 (38.7) mmHg, p<0.0001 at 12 weeks, -51.1 (35.3) mmHg, p<0.0001 at 24 weeks). These reductions started to occur within two weeks of treatment, were sustained through 24 weeks of treatment, and were achieved with only modest decreases in the average LVEF (-3.2 (4.2) %, p=0.0038 at 24 weeks). Compared to baseline (47% Class II, 53% Class III), New York Heart Association (NYHA) Functional Class was improved in the majority of patients (p<0.0001 for improvement by one or more NYHA class), and no patients had a worsening of NYHA Class. At 12 weeks, 72% of patients improved by one class and 7% improved by two classes; at 24 weeks 61% of patients improved by one class and 17% improved by two classes. For patients reaching Week 24, 56% were Class I and 39% were Class II. There were also significant improvements in cardiac biomarkers including NTpro-BNP (reduction of 70% from baseline, p<0.001) and cardiac troponin (20% reduction, p=0.002). Treatment with *aficamten* was well-tolerated with one temporary discontinuation due to LVEF <50% and one temporary down-titration, neither related to drug. Both patients remain on treatment with *aficamten.*

GALACTIC-HF: Patients with Low Blood Pressure Treated with *Omecamtiv Mecarbil* Have an Increased Treatment Effect

Marco Metra, M.D., Professor of Cardiology & Director of the Institute of Cardiology, Department of Medical & Surgical Specialties, Radiological Sciences & Public Health, University & Civil Hospitals of Brescia, Italy presented an analysis from GALACTIC-HF on the effect of treatment with *omecamtiv mecarbil* in patients with HFrEF and low blood pressure. Of 8,232 patients with available baseline data on blood pressure, 1,473 patients (17.9%) had low systolic blood pressure defined as ≤100 mmHg. All patients with low blood pressure had an increased risk of cardiovascular death or heart failure events compared to patients without low blood pressure. In patients with low blood pressure, there was a greater treatment effect from *omecamtiv mecarbil* on the primary composite endpoint of cardiovascular death or first heart failure event than in patients without low blood pressure such that there was an absolute risk reduction of 9.8 events per 100 patient-years (hazard ratio, 0.81; 95% confidence interval [CI] 0.70, 0.94; interaction p=0.051). Patients with low blood pressure treated with *omecamtiv mecarbil* also experienced improvements in blood pressure over time as did those treated with placebo. Additionally, the incidence of treatment-emergent serious adverse events in patients with low blood pressure who received *omecamtiv mecarbil* (RR 0.88; 95% CI 0.82, 0.95; p<0.001) and adjudicated first stroke (RR 0.31; 95% CI 0.12, 0.79; p=0.009) was lower compared to placebo. Other measures of safety and tolerability were also similar between patients with low blood pressure and those without low blood pressure.

GALACTIC-HF: Treatment Effect of *Omecamtiv Mecarbil* on Primary Outcome Consistent in Patients with or without Tricuspid Regurgitation

Marianna Adamo, M.D., Interventional Cardiologist, University of Brescia, Italy presented an analysis from GALACTIC-HF on the impact of tricuspid regurgitation (TR) on the effectiveness of *omecamtiv mecarbil*. Of 8,256 patients in GALACTIC, 8,180 patients had data reported on TR, of which 6,476 (79%) had no TR, 919 (11%) had mild TR, and 785 (10%) had moderate/severe TR. Compared to patients with no TR, patients with moderate/severe TR were older (p=0.003), more often enrolled in an inpatient setting (p<0.001), had higher incidence of atrial fibrillation or flutter (p<0.001), were a worse NYHA functional class (p<0.001), had higher heart rate (p<0.001), and had worse cardiac biomarker levels including higher NT-proBNP and higher cardiac troponin (p<0.001 for both). Baseline moderate/severe TR was also associated with lower KCCQ Total Symptom

Scores, an indicator of lower quality of life. Patients with moderate/severe TR in GALACTIC-HF experienced higher rates of the primary composite endpoint, cardiovascular death, all-cause death and heart failure events. The impact of moderate/severe TR on heart failure events was more pronounced in outpatients and in patients with higher LVEF, lower NT-proBNP and lower eGFR. The treatment effect of *omecamtiv mecarbil* on the primary outcome was consistent across patients with no TR, mild TR and moderate/severe TR such that baseline TR did not modify the treatment effect (interaction p=0.91).

About *Aficamten*

Aficamten is an investigational selective, small molecule cardiac myosin inhibitor discovered following an extensive chemical optimization program that was conducted with careful attention to therapeutic index and pharmacokinetic properties and as may translate into next-in-class potential in clinical development. *Aficamten* was designed to reduce the number of active actin-myosin cross bridges during each cardiac cycle and consequently suppress the myocardial hypercontractility that is associated with hypertrophic cardiomyopathy (HCM). In preclinical models, *aficamten* reduced myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state. The development program for *aficamten* is assessing its potential as a treatment that improves exercise capacity and relieves symptoms in patients with HCM as well as its long-term effects on cardiac structure and function. *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic obstructive HCM from the U.S. Food & Drug Administration (FDA) as well as the National Medical Products Administration (NMPA) in China.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a disease in which the heart muscle (myocardium) becomes abnormally thick (hypertrophied). The thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller and stiffer, and thus the ventricle becomes less able to relax and fill with blood. This ultimately limits the heart's pumping function, resulting in symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. A subset of patients with HCM are at high risk of progressive disease which can lead to atrial fibrillation, stroke and death due to arrhythmias. There are no FDA approved medical treatments that directly address the hypercontractility that underlies HCM.

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* is 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.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide[5] about half of whom have reduced left ventricular function.[6,7] It is the leading cause of hospitalization and readmission in people age 65 and older.[8,9] Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.[10] 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.[11,12] More than 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have severe heart failure.[13]

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 any of our other clinical trials, including statements relating to the potential benefits of *aficamten* for patients with obstructive hypertrophic cardiomyopathy and statements relating to the potential benefits of *omecamtiv mecarbil* for patients with heart failure with reduced ejection fraction. 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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