Cytokinetics Receives Complete Response Letter From FDA for New Drug Application for Omecamtiv Mecarbil

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Complete Response Letter States that GALACTIC-HF Alone Does not Establish Substantial Evidence of Effectiveness Sufficient for Approval

Company Expects to Request Meeting with FDA to Discuss Potential Next Steps

Cytokinetics to Host Conference Call and Webcast on March 1, 2023 at 8:30 am Eastern Time

SOUTH SAN FRANCISCO, Calif., Feb. 28, 2023 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the U.S. Food and Drug Administration (FDA) issued a Complete Response Letter (CRL) regarding the New Drug Application (NDA) for *omecamtiv mecarbil*, an investigational, selective, small molecule cardiac myosin activator, for the treatment of heart failure with reduced ejection fraction (HFrEF).

FDA communicated that GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with reduced ejection fraction, in lieu of evidence from at least two adequate and well-controlled clinical investigations. FDA stated that results from an additional clinical trial of *omecamtiv mecarbil* are required to establish substantial evidence of effectiveness for the treatment of HFrEF, with benefits that outweigh the risks. 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) was a Phase 3 clinical trial of *omecamtiv mecarbil* that enrolled patients with HFrEF at risk of hospitalization and death, despite being treated with standard-of-care therapy.

Cytokinetics expects to request a meeting with FDA in order to understand FDA's views regarding the CRL and what may be required to support potential approval of *omecamtiv mecarbil*. However, the Company has no plans to conduct an additional clinical trial of *omecamtiv mecarbil* and its focus remains on the development program for *aficamten*, the next-in-class cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, a Phase 3 clinical trial in patients with obstructive hypertrophic cardiomyopathy (HCM).

"We are disappointed with this outcome, especially considering the high unmet need for innovative treatments for patients suffering from worsening heart failure," said Robert I. Blum, Cytokinetics' President & Chief Executive Officer. "We are humbled by the support of the heart failure community and will engage with FDA and consider what may be next steps for *omecamtiv mecarbil* in the U.S. In parallel, we look forward to continuing a broad development program for *aficamten*, with expected results from SEQUOIA-HCM and the start of two more Phase 3 clinical trials later this year."

Conference Call and Webcast

Cytokinetics will host a conference call tomorrow, March 1, 2023 at 8:30 AM Eastern Time that will be simultaneously webcast and can be accessed from the homepage and in the Investors & Media section of Cytokinetics' website at www.cytokinetics.com. The live audio of the event can also be accessed by telephone by registering in advance at the following link: ***Omecamtiv Mecarbil* Regulatory Update Call**. Upon registration, participants will receive a dial-in number and a unique passcode to access the call.

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* assessed 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% of people diagnosed with heart failure will die within five years of initial hospitalization.[11,12] Approximately 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have worsening 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 developing *omecamtiv mecarbil*, a cardiac muscle activator in patients with heart failure. Cytokinetics is also developing *aficamten*, a next-in-class 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). In 2023, Cytokinetics is celebrating its 25-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, express or implied, relating to the Company's development plans for *omecamtiv mecarbil* in the United States. 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