

Cytokinetics Announces Preclinical Data Relating to CK-3828136 Presented at the 2021 Medicinal Chemistry Gordon Research Conference

October 29, 2021 11:30 AM EDT

SOUTH SAN FRANCISCO, Calif., Oct. 29, 2021 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that preclinical data relating to the discovery and optimization of CK-3828136 (CK-136) were presented at the 2021 Medicinal Chemistry Gordon Research Conference in West Dover, VT. CK-136 is a novel, selective cardiac troponin activator in development for the potential treatment of diseases associated with impaired cardiac contractility, such as heart failure with reduced ejection fraction (HFrEF), right ventricular heart failure, and others.

"There is substantial evidence showing that activating cardiac myosin augments cardiac contractility and improves the clinical outcomes of patients, suggesting that activating the cardiac sarcomere is a viable approach to treat heart failure. We are developing an activator of cardiac troponin that also selectively increases cardiac function without increasing intracellular myocyte calcium concentrations," said Brad Morgan, Ph.D., Cytokinetics' Senior Vice President, Research and Non-Clinical Development. "CK-136 appears to have a favorable pharmacodynamic window that may provide for meaningful increases in cardiac function supportive of further clinical research to investigate its mechanism of action in diseases characterized by reduced cardiac function."

Data presented today describe the primary research objectives related to CK-136 including the identification of initial hit compounds and subsequent chemical optimization as well as preclinical characterization in biochemical assays, cardiac myocytes, and *in vivo* models of cardiac function. An initial cardiac troponin activator identified in screening was shown in a reconstituted sarcomere assay to selectively activate the cardiac troponin complex. Importantly, it did not inhibit phosphodiesterase 3 (PDE-3) and showed no effect on the cardiomyocyte calcium transient, indicating its selectivity. The optimization of the initial hit compound that led to CK-136 focused to maximizing the therapeutic window and its pharmacokinetic profile as could result in favorable increases in cardiac function. Preclinical studies demonstrated that the pharmacodynamic range for CK-136 was larger than that associated with *omecantiv mecarbil* in similar preclinical models. Additionally, CK-136 demonstrated a pharmacokinetic profile and a projected human half-life that should enable once or twice daily dosing.

These preclinical data suggest that CK-136 is a selective cardiac troponin activator with a favorable pharmacodynamic window associated with substantial increases in cardiac contractility, representing a potential approach to augmenting cardiac contractility in diseases characterized by reduced cardiac function.

About CK-136

CK-136 is an investigational, selective, small molecule cardiac troponin activator. In preclinical models, CK-136 increases myocardial contractility by binding to cardiac troponin through an allosteric mechanism that sensitizes the cardiac sarcomere to calcium, facilitating more actin-myosin cross bridge formation during each cardiac cycle, thereby resulting in increased myocardial contractility. Similar to cardiac myosin activation, preclinical research has shown that cardiac troponin activation does not change the calcium transient of cardiac myocytes. The development program for CK-136 is assessing its potential for the treatment of diseases associated with impaired cardiac contractility, such as heart failure with reduced ejection fraction (HFrEF), right ventricular heart failure, and others.

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 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 *aficamten*, a next-generation cardiac myosin inhibitor, for the potential treatment of hypertrophic cardiomyopathies (HCM). The company has announced positive results from Cohorts 1 and 2 in REDWOOD-HCM, a Phase 2 clinical trial of *aficamten* in patients with obstructive HCM. Cytokinetics is also developing *reldesentiv*, a fast skeletal muscle troponin activator, currently the subject of COURAGE-ALS, a Phase 3 clinical trial in patients with ALS. Cytokinetics is 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 Cytokinetics' and its partners' research and development activities; the timing of enrollment of patients in Cytokinetics' and its partners' clinical trials; the design, timing, results, significance and utility of preclinical and clinical results; and the properties and potential benefits of Cytokinetics' 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; patient enrollment for or conduct of clinical trials may be difficult or delayed; 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; Cytokinetics' partners decisions with respect to research and development activities; 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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