



Cytokinetics Announces Preclinical Data for CK-3773274 and CK-3772271 Presented at the AHA Scientific Sessions 2020

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New Findings from Studies of Cardiac Myosin Inhibitors in Animal Models of Hypertrophic Cardiomyopathy and Heart Failure with Preserved Ejection Fraction

SOUTH SAN FRANCISCO, Calif., Nov. 16, 2020 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: [CYTK](#)) today announced that preclinical data for CK-3773274 (CK-274) and CK-3772271 (CK-271) were shared in poster presentations at the American Heart Association (AHA) Scientific Sessions 2020. CK-274 reduced contractility and left ventricular outflow tract (LVOT) peak pressure gradient in cats with naturally occurring hypertrophic cardiomyopathy (HCM) and left ventricular outflow tract obstruction (LVOTO). In the Dahl/Salt sensitive rat model of heart failure with preserved ejection fraction (HFpEF), CK-271 attenuated the development of fibrosis and diastolic dysfunction.

"We're pleased to share preclinical data that builds on the growing body of evidence for our pipeline of cardiac myosin inhibitors," said Brad Morgan, Ph.D., Cytokinetics' Senior Vice President, Research and Non-Clinical Development. "Collectively, these data demonstrate the potential of this mechanism of action to reduce or arrest the development of cardiac hypercontractility in animal models which may support application in patients with diseases of hypercontractility including HCM and HFpEF."

Previous preclinical data has shown that CK-274 produces exposure related effects on cardiac contractility in healthy animals and mouse models of HCM. New preclinical data demonstrated dose-related changes in left ventricular (LV) systolic function and reductions in LVOT peak pressure gradient in cats with naturally occurring HCM and LVOTO due to the A31P mutation in cardiac myosin binding protein C (cMyBP-C). Treatment with CK-274 (1 mg/kg) reduced mean left ventricular (LV) fractional shortening at 6, 24, and 48 hours post-treatment (mean reduction 13.6%, $p = 0.03$; 15.4%, $p = 0.01$; 11.6%, $p = 0.02$, respectively). In addition to lowering the hypercontractility in cats with naturally occurring HCM and LVOTO, CK-274 reduced the left ventricular outflow tract peak pressure gradient in concentration related manner (median pressure gradient at baseline 27.1 mmHg [interquartile range {IQR} 18.3–33.3] vs 24 hours post-drug, 7.3 mmHg [IQR 14.2–19.7], $p = 0.01$). CK-274 was well tolerated and no changes in heart rate were observed for any treatment group over time.

A preclinical study of CK-271 demonstrated that treatment with this novel small molecule cardiac myosin inhibitor attenuated the development of fibrosis and diastolic dysfunction in an animal model of HFpEF. Previous studies have shown that CK-271 reduces cardiac myosin ATPase activity *in vitro* and cardiac contractility *in vivo* in healthy rats and dogs. In this study of the Dahl/Salt Sensitive rat hypertension model of HFpEF, six weeks of treatment with CK-271 reduced fractional shortening (HS: 53.8 ± 1.4 vs HS + CK-271: $42.7 \pm 1.0\%$, $p < 0.0001$) and reduced high salt diet-induced diastolic dysfunction, including reductions in isovolumic relaxation time (IVRT) (HS: 22.8 ± 0.6 vs HS + CK-271: 19.5 ± 0.5 ms, $p < 0.0001$) and left atrial area (HS: 42.5 ± 2.2 vs HS + CK-271: 35.4 ± 0.8 mm², $p < 0.0001$). CK-271 also reduced the development of cardiac fibrosis induced by a high salt diet (HS: 5.0 ± 0.6 vs HS + CK-271: $3.5 \pm 0.3\%$, $p < 0.05$). These results suggest that cardiac myosin inhibition may be a novel approach to mitigate the development of HFpEF.

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 collaborating with Amgen Inc. (Amgen) to develop *omecantiv mecarbil*, a novel cardiac muscle activator. *Omecantiv mecarbil* is the subject of an international clinical trials program in patients with heart failure including GALACTIC-HF, of which topline results were recently reported, and METEORIC-HF, which is ongoing. Amgen holds an exclusive worldwide license to develop and commercialize *omecantiv mecarbil* with a sublicense held by Servier for commercialization in Europe and certain other countries. Cytokinetics is developing *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA) 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 is collaborating with Astellas Pharma Inc. (Astellas) to research, develop and commercialize other novel mechanism skeletal sarcomere activators (not including FSTAs). Licenses held by Amgen and Astellas are subject to specified co-development and co-commercialization rights of Cytokinetics. Cytokinetics is also developing CK-274, a novel cardiac myosin inhibitor that company scientists discovered independent of its collaborations, for the potential treatment of hypertrophic cardiomyopathies. Cytokinetics has granted Ji Xing Pharmaceuticals Limited an exclusive license to develop and commercialize CK-274 in China and Taiwan, in accordance with Cytokinetics' planned global registration programs. Cytokinetics is conducting REDWOOD-HCM, a Phase 2 clinical trial of CK-274 in patients with obstructive HCM. 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 timing, design and results of Cytokinetics' preclinical trials of CK-274 or CK-271; the potential benefits of CK-274 or CK-271; 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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