Cytokinetics Announces Preclinical Data for AMG 594 Presented at the Keystone Symposium on Heart Failure

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In Vitro Studies Demonstrate Cardiac Troponin Activator Selectively Activates Cardiac Muscle Fibers with Little Effect on Slow Skeletal Muscle or Fast Skeletal Muscle

Expect to Complete SAD/MAD Phase 1 Study of AMG 594 in 2H 2020

SOUTH SAN FRANCISCO, Calif., March 03, 2020 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that preclinical data related to AMG 594 were presented at the Keystone Symposium "Charting a New Course for Heart Failure: From Discovery to Data," in Keystone, Colo., characterizing its mechanism of action and effect to increase cardiac contractility. AMG 594 is a novel mechanism cardiac troponin activator, discovered under a joint research program conducted between Amgen and Cytokinetics.

"We are pleased to share *in vitro* findings that demonstrate AMG 594 increases calcium sensitivity of cardiac muscle fibers and increases cardiac contractility, supporting the approach of cardiac troponin activation to potentially treat diseases characterized by reduced cardiac function," said Bradley Morgan, Ph.D., Cytokinetics' Senior Vice President, Research and Non-Clinical Development. "*In vivo* results also suggest that the pharmacodynamic window of AMG 594 may be favorable and we expect to complete the SAD/MAD Phase 1 study of AMG 594 in the second half of this year."

Preclinical *In Vitro* Research

Several *in vitro* studies demonstrated that AMG 594 selectively increased the calcium sensitivity of the troponin complex in cardiac muscle. In bovine cardiac myofibrils, AMG 594 increased activation by calcium in a concentration-dependent manner. This activation was selective when compared to myofibrils from fast and slow skeletal muscle. Additionally, in experiments using a reconstituted hybrid sarcomere, AMG 594 selectively targeted the cardiac troponin complex over the fast or slow skeletal muscle troponin complex. In intact cardiac muscle fibers, AMG 594 increased calcium sensitivity and maximal isometric tension in a concentration-dependent manner. Additionally, in cardiac myocytes, AMG 594 increased fractional shortening (FS), a measure of cardiac contractility, without any effect on the calcium transient.

Preclinical *In Vivo* Research

In vivo studies demonstrated a pharmacodynamic window of AMG 594 that was associated with substantial increases in cardiac contractility. Echocardiographic assessments in healthy rats, myocardial infarcted rats, and healthy dogs showed that an intravenous infusion of an escalating dose of AMG 594 was associated with exposure-dependent increases in measures of FS and ejection fraction (EF) that were driven primarily by a reduction in left ventricular end systolic dimensions.

These data demonstrate that AMG 594 selectively increased cardiac contractility *in vitro* and *in vivo*, suggesting that cardiac troponin activation is a viable approach to augment cardiac contractility in diseases characterized by reduced cardiac function.

About AMG 594

AMG 594 is a novel, selective, oral, small molecule cardiac troponin activator discovered under our joint research program with Amgen. In preclinical models, AMG 594 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. Development of AMG 594 may include the evaluation of this novel mechanism of action as a potential treatment of patients with heart failure with reduced ejection fraction (HFrEF) and other types of heart failure, such as right ventricular failure, resulting from impaired cardiac contractility.

About Cytokinetics and Amgen Collaboration

In 2006, Cytokinetics and Amgen entered into a strategic alliance to discover, develop and commercialize novel small molecule therapeutics designed to activate the cardiac sarcomere for the potential treatment of heart failure. *Omecamtiv mecarbil*, a cardiac myosin activator, and AMG 594, a cardiac troponin activator, are being developed by Amgen in collaboration with Cytokinetics. Amgen holds an exclusive, worldwide license to *omecamtiv mecarbil* and AMG 594, subject to Cytokinetics' specified development and commercialization rights. Cytokinetics is eligible for pre-commercialization and commercialization milestone payments and royalties that escalate based on increasing levels of annual net sales of products commercialized under the agreement. Amgen has also entered an alliance with Servier for exclusive commercialization rights for *omecamtiv mecarbil* in Europe as well as the Commonwealth of Independent States, including Russia. Servier contributes funding for development and provides strategic support to the program for *omecamtiv mecarbil*. Servier is an independent international pharmaceutical company, governed by a non-profit foundation, with its headquarters in France.

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 *omecamtiv mecarbil*, a novel cardiac muscle activator, and AMG 594, a novel cardiac troponin activator. *Omecamtiv mecarbil* is the subject of an international clinical trials program in patients with heart failure including GALACTIC-HF and METEORIC-HF. Amgen holds an exclusive worldwide license to develop and commercialize *omecamtiv mecarbil* with a sublicense held by Servier for commercialization in Europe and certain other countries. Cytokinetics is collaborating with Astellas Pharma Inc. (Astellas) to develop *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA). Astellas currently holds an exclusive worldwide license to develop and commercialize *reldesemtiv*. 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 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 Amgen's Phase 1 clinical trial of AMG 594; the potential benefits of AMG 594; 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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