Cytokinetics Announces Publication Relating to Novel Smooth Muscle Myosin Inhibitor

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Discovery of Novel Binding Mechanism Has Potential to Guide Design of Myosin Inhibitors

SOUTH SAN FRANCISCO, Calif., Nov. 07, 2016 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK) a leader in muscle biology and the mechanics of muscle performance, today announced the publication of preclinical data characterizing a smooth muscle myosin (SMM) inhibitor that induces smooth muscle relaxation. The manuscript titled, "Highly Selective Inhibition of Myosin Motors Provides the Basis of Potential Therapeutic Application," published in PNAS, Proceedings of the National Academy of Sciences, illustrates a mechanism of action with potential relevance for diseases of smooth muscle hypercontractility such as asthma and chronic obstructive pulmonary disease. The research was conducted in collaboration with Anne Houdusse, Institut Curie, Paris, France.

"We are continually interested in understanding the basis by which small molecule compounds modulate myosin function and characterizing the diversity of their mechanisms," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President, Research & Development. "This study is particularly interesting in that we have revealed a new mechanistic approach that may have application across a diversity of myosin inhibitors and distinguishes the binding site for these compounds from comparable compounds that may promote contractility. Importantly, the newly identified allosteric binding site on myosin has the potential to guide the design of novel class-specific myosin inhibitors."

The objective of the study was to define the mechanism of the SMM inhibitor, CK-2018571 (CK-571), and the structural basis that underlies its inhibition of this motor protein. The inhibitory mechanism of CK-571 was elucidated by defining the enzymatic step in which the compound traps the motor and the subsequent determination of the high-resolution structure of SMM co-crystallized with CK-571. The authors found that the compound targets an intermediate state that occurs during the myosin recovery stroke, the large conformational rearrangement that enables re-priming of the motor. Blocking this critical transition appears to result in efficient inhibition of force production. Furthermore, the atomic structure of CK-571 and the SMM complex shows that the compound binds in an allosteric pocket of the myosin motor that forms transiently during its recovery stroke - one that has not been found in previously described structures of the motor. By stabilizing an enzymatic state that can neither hydrolyze ATP nor bind actin, CK-571 prevents smooth muscle myosin from participating in mechanical force production. As the authors state, "CK-571 exemplifies an innovative and efficient mechanism to achieve complete relaxation of smooth muscle."

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators 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 increase muscle function and contractility. Cytokinetics' lead drug candidate is *tirasemtiv*, a fast skeletal muscle troponin activator, for the potential treatment of ALS. *Tirasemtiv* has been granted orphan drug designation and fast track status by the U.S. Food and Drug Administration and orphan medicinal product designation by the European Medicines Agency for the potential treatment of ALS. Cytokinetics retains the right to develop and commercialize *tirasemtiv*, subject to an option held by Astellas Pharma Inc. Cytokinetics is also collaborating with Astellas to develop CK-2127107, a fast skeletal muscle activator, for the potential treatment of spinal muscular atrophy, chronic obstructive pulmonary disease and ALS. Cytokinetics is collaborating with Amgen Inc. to develop *omecamtiv mecarbil*, a novel cardiac muscle activator, for the potential treatment of heart failure. Amgen holds an exclusive license worldwide to develop and commercialize *omecamtiv mecarbil* and Astellas holds an exclusive license worldwide to develop and commercialize CK-2127107. Both licenses are subject to Cytokinetics' specified development and commercialization participation rights. For additional information about Cytokinetics, visit http://www.cytokinetics.com/.

About Institut Curie

Institut Curie, a private, non-profit foundation, is one of the leading medical, biological and biophysical research centres in the world. Anne Houdusse is an international expert in molecular motors and small GTPases effectors, in particular as a structural biologist. A major focus of the Structural Motility Laboratory she directs is to use X-ray crystallography to solve atomic structures that help understand how myosin motors produce force and how their activity can be modulated. For additional information, visit http://bit.ly/2fkguA8.

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 potential for Cytokinetics' technology platforms and the properties and potential efficacy and safety profile 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, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results; 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 may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; 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; 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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