Cytokinetics Announces Four Research Posters at the 46th Annual American Society for Cell Biology Meeting

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Data Presented Advance Scientific Insights in Cytoskeletal Pharmacology

SOUTH SAN FRANCISCO, Calif., Dec. 13 /PRNewswire-FirstCall/ -- Cytokinetics, Incorporated (Nasdaq: CYTK -) announced today that four posters relating to the company's research activities were presented this week at the 46th Annual American Society for Cell Biology (ASCB) Meeting in San Diego, California.

The following posters were presented:

-- "A Novel Mechanism for Kinesin Spindle Protein (KSP) Modulation: Small Molecular Activators of KSP Basal ATPase," was presented on Monday, December 11, 2006. This presentation covered experiments focused to developing a highly sensitive coupled enzymatic ADP formation assay. This presentation concluded that the basal ATPase activity of KSP can be screened using a sensitive readout of ADP generation yielding several series of compounds that inhibit the basal and microtubule-stimulated KSP ATPase activities. A series of compounds that activate the KSP basal ATPase but inhibit its microtubule-stimulated ATPase were demonstrated to cause mitotic arrest with monopolar spindles. These compounds may represent a distinct means of perturbing KSP function in spindle pole separation and mitotic progression.
-- "Functional Studies of Human Kip3D (Kif18A) Kinesin," was presented on Monday, December 11, 2006. This presentation covered experiments characterizing one member of the Kip3 family, human Kip3D. This presentation concluded that Kip3D localizes to ends of mitotic spindle microtubules and is a microtubule depolymerizing kinesin. Kip3D function appears most important during mitosis, where siRNA knockdown results in mitotic arrest and activation of Caspase 3 and possibly apoptosis.
-- "Characterization of Motor-Domain Mutants of the Mitotic Kinesin RAB6KIFL (MKLP2, KIF20A)," was presented on Monday, December 11, 2006. This presentation covered experiments that engineered and characterized three motor domain mutants of RAB6KIFL: T167N (P-loop), R379A (Switch I), and G411A (Switch II), in order to explore the relationship between the biochemical activity and biological function of this motor protein. It was concluded that all three mutants lack ATPase activity. In addition, T167N does not bind microtubules, while binding by R379A and G411A is significantly different from the wild-type protein. The wild-type and mutant constructs localize to the central spindle microtubules. The R379A and G411A mutants, however, are broadly distributed along the central spindle and not concentrated in the midzone like the wild-type protein. This presentation concluded that an inhibitor of the RAB6KIFL ATPase would be likely to disrupt the recruitment to the central spindle of critical kinases such as Plk-1 and Aurora-B.
-- "Effects of the Cardiac Myosin Activator CK-1316719 on Excitation-Contraction (E-C) Coupling in Ventricular Myocytes," was presented on

Wednesday, December 13, 2006. This presentation covered experiments that examined aspects of E-C coupling in adult rat cardiac myocytes after treatment with the cardiac myosin activator CK-1316719. The presentation concluded that CK-1316719 increases contractility in a dose-responsive manner without increasing intracellular calcium, without changing sarcoplasmic reticulum calcium content and without altering the sodium calcium exchanger. These data support the proposed mechanism of action of cardiac myosin activators, namely increasing contractility by directly activating cardiac myosin, with no effects on other aspects of E-C coupling including calcium dynamics.

"We are pleased to have the opportunity to present these non-clinical data from our cell cycle control and contractility research programs," stated David J. Morgans, Jr., Ph.D., Cytokinetics' Senior Vice President of Drug Discovery and Development. "These presentations demonstrate our continuing efforts to maintain and strengthen our focus and advance our scientific insights in the area of cytoskeletal biology and pharmacology."

About Cytokinetics

Cytokinetics is a biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule drugs that specifically target the cytoskeleton. The cytoskeleton is a complex biological infrastructure that plays a fundamental role within every human cell. Cytokinetics' focus on the cytoskeleton enables it to develop novel and potentially safer and more effective classes of drugs directed at treatments for cancer, cardiovascular disease and other diseases. Under a strategic alliance established in 2001, Cytokinetics and GlaxoSmithKline (GSK) are conducting research and development activities focused towards the potential treatment of cancer and other indications. Cytokinetics and GSK are continuing collaborative research focused to translational research directed to the mitotic kinesin centromere-associated protein E (CENP-E). GSK-923295, a CENP-E inhibitor, is being developed under the strategic alliance by GSK; GSK expects to begin clinical trials with GSK-923295 in 2007. Cytokinetics is responsible for the development of ispinesib and SB-743921, each a novel inhibitor of the mitotic kinesin KSP. Ispinesib has been the subject of a broad clinical trials program comprised of nine Phase II clinical trials as well as eight Phase I or Ib clinical trials. Cytokinetics plans to conduct additional clinical trials with ispinesib and is conducting a Phase I/II trial of SB-743921 in non-Hodgkin's lymphoma. Cytokinetics' unpartnered cardiovascular disease program is the second program to leverage the company's expertise in cytoskeletal pharmacology. Cytokinetics recently completed a Phase I clinical trial with CK-1827452, a novel small molecule cardiac myosin activator, and is advancing CK-1827452 in both intravenous and oral formulations for the treatment of heart failure. Additional information about Cytokinetics can be obtained at http://www.cytokinetics.com .

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