



Cytokinetics Announces Clinical Trial Data Regarding SB-743921 Presented at the 2008 Annual Meeting of American Society of Hematology

December 8, 2008 12:32 PM EST

SOUTH SAN FRANCISCO, CA, Dec 08, 2008 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that an abstract summarizing interim Phase I data from a clinical trial evaluating SB-743921 in patients with lymphoma was presented as a poster at the 2008 Annual Meeting of the American Society of Hematology (ASH) held on December 6-9, 2008 at the Moscone Center in San Francisco, California. SB-743921 is a novel, small molecule inhibitor of kinesin spindle protein (KSP), a mitotic kinesin essential for proper cell division, being developed by Cytokinetics in collaboration with GlaxoSmithKline.

Poster Presentation at ASH

A poster entitled, "A Phase I/II Trial of the Kinesin Spindle Protein (KSP) Inhibitor SB-743921 Administered on Days 1 and 15 Every 28 Days without and with Prophylactic G-CSF in Non-Hodgkin or Hodgkin Lymphoma" was presented on Saturday, December 6, 2008 by John Gerecitano, MD, PhD of the Memorial Sloan-Kettering Cancer Center, New York, NY. The primary objectives of the Phase I portion of this clinical trial are to determine the dose-limiting toxicities (DLTs) and maximum tolerated dose (MTD) and to assess the safety and tolerability of SB-743921 administered as a 1-hour intravenous infusion on days 1 and 15 of a 28-day cycle, first without and then with the prophylactic administration of granulocyte colony-stimulating factor (G-CSF). The secondary objectives are to characterize the pharmacokinetics of SB-743921 administered on this schedule and to evaluate the effect of SB-743921 on biomarkers of cell proliferation in patients with accessible tumors.

At this interim analysis point, 51 patients had been treated; all were evaluable for safety and 43 were evaluable for efficacy. The MTD of SB-743921 was 6 mg/m² when given days 1 and 15 every 28 days without prophylactic G-CSF support. This represents a greater dose density (0.43 mg/m²/day) than was achieved on the previously studied schedule; i.e., 4 mg/m² once every 21 days (0.19 mg/m²/day). The main DLT observed without G-CSF was neutropenia; therefore, further dose escalation with empiric, prophylactic G-CSF was initiated and is ongoing. The trial is currently enrolling at 9 mg/m² with prophylactic G-CSF support. Grade 3 and 4 toxicities other than neutropenia were uncommon; in particular, no evidence of neuropathy or alopecia greater than Grade 1 was observed. To date, two partial responses have been observed at doses at or above 6 mg/m², both in patients with Hodgkin lymphoma.

"These data are encouraging for SB-743921 as a potential novel drug for the treatment of patients with lymphoma," stated Dr. Gerecitano. "The favorable tolerability profile of SB-743921 combined with the preliminary signal of clinical activity in this Phase I portion of this clinical trial is encouraging as dose escalation with this new dosing schedule with G-CSF support continues."

"Based on the time course of the onset and recovery of neutropenia in the previous study, in which SB-743921 was administered every 21 days, we hypothesized we might be able to increase the dose density while maintaining a favorable tolerability profile by giving SB-743921 on days 1 and 15 of a 28-day cycle," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "These data support this hypothesis, and demonstrate this novel KSP inhibitor may play an important role as a novel anti-mitotic in the treatment of refractory lymphoma."

Development Status of SB-743921

In June and October 2008, Cytokinetics reported interim data from the Phase I portion of this Phase I/II clinical trial of SB-743921. The authors of these poster presentations observed that SB-743921 was well-tolerated at the doses being reported at that time and concluded that the pattern of neutropenia onset and recovery supported a dosing schedule for SB-743921 of days 1 and 15 of a 28-day cycle. The major DLT observed without G-CSF was neutropenia; therefore, further dose escalation with empiric, prophylactic G-CSF was initiated and is ongoing. In May 2006 at the American Society of Clinical Oncology (ASCO) annual meeting, GSK presented data from an open-label, non-randomized, dose-finding Phase I clinical trial of SB-743921 administered as a 1-hour intravenous infusion once every 21 days to patients with advanced solid tumors. In that study, SB-743921 appeared to have an acceptable tolerability profile. Similarly, the main DLT reported on a once-every-21 days schedule was prolonged neutropenia.

Background on Mitotic Kinesin Inhibitors

Since their introduction over 40 years ago, anti-mitotic drugs (taxanes and vinca alkaloids) have advanced the treatment of cancer and are commonly used for the treatment of several tumor types. However, these drugs have demonstrated limited treatment benefit against certain cancers. In addition, these drugs target tubulin, a cytoskeletal protein involved not only in mitosis and cell proliferation, but also in other important cellular functions. Inhibition of these other cellular functions produces dose-limiting toxicities such as peripheral neuropathy, an impairment of peripheral nervous system function. Neuropathies are thought to result when these drugs interfere with the dynamics of microtubule filaments that are responsible for the long-distance transport of important cellular components within nerve cells.

Mitotic kinesins are essential to mitosis, and, unlike tubulin, are not believed to be present in non-dividing cells. Cytokinetics believes that drugs that inhibit KSP, centromere-associated protein E, (CENP-E) and other mitotic kinesins may represent the next generation of anti-mitotic cancer drugs by arresting mitosis and cell proliferation without impacting unrelated, normal cellular functions, thereby avoiding many of the toxicities commonly experienced by patients treated with existing anti-mitotic drugs.

KSP is a mitotic kinesin which acts at the earliest stage of spindle formation. Early in mitosis, during prophase, KSP forces the emerging spindle poles to move apart, driving formation of a bipolar spindle and enabling chromosome segregation into two resultant daughter cells. KSP is not expressed in neurons and has only one known function, to drive spindle pole separation during mitosis. Inhibition of KSP motor function prevents formation of a bipolar spindle. KSP inhibition results in cell cycle arrest in mitosis with a characteristic monopolar spindle on which chromosomes are arrayed. In cancer cells, duplicated chromosomes remain attached to this monopolar spindle in a persistent state of cell cycle arrest, resulting in programmed cell

death, or apoptosis.

CENP-E plays an essential role in chromosome movement during early mitosis and integrates mitotic spindle mechanics with regulators of the mitotic checkpoint; hence CENP-E is directly involved in coupling the mechanics of mitosis with the mitotic checkpoint signaling machinery, regulating cell-cycle transition from metaphase to anaphase. CENP-E is also essential for prometaphase chromosome movements that contribute to metaphase chromosome alignment. These processes are essential to cell proliferation. CENP-E is expressed exclusively in proliferating cells and is abundant during mitosis; it is absent from non-proliferating cells, including neurons. Inhibition of CENP-E induces cell cycle arrest in mitosis with bipolar mitotic spindles and misaligned chromosomes leading to subsequent apoptosis.

About Cytokinetics

Cytokinetics is a biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule drugs that may address areas of significant unmet clinical needs. Cytokinetics' cardiovascular disease program is focused on cardiac myosin, a motor protein essential to cardiac muscle contraction. Cytokinetics' lead compound from this program, CK-1827452, a novel small molecule cardiac myosin activator, entered Phase II clinical trials for the treatment of heart failure in 2007. Under a strategic alliance established in 2006, Cytokinetics and Amgen Inc. are performing joint research focused on identifying and characterizing activators of cardiac myosin as back-up and follow-on potential drug candidates to CK-1827452. Amgen has obtained an option for an exclusive license to develop and commercialize CK-1827452, subject to Cytokinetics' development and commercial participation rights. Cytokinetics' cancer program is focused on mitotic kinesins, a family of motor proteins essential to cell division. Under a strategic alliance established in 2001, Cytokinetics and GlaxoSmithKline (GSK) are conducting research and development activities focused on the potential treatment of cancer. Cytokinetics is developing two novel drug candidates that have arisen from this program, ispinesib and SB-743921, each a novel inhibitor of kinesin spindle protein (KSP), a mitotic kinesin. Cytokinetics is conducting the Phase I portion of a Phase I/II clinical trial of ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer. In addition, Cytokinetics is conducting the Phase I portion of a Phase I/II trial of SB-743921 in patients with non-Hodgkin or Hodgkin lymphoma. GSK has an option for the joint development and commercialization of ispinesib and SB-743921. GSK-923295, an inhibitor of centromere-associated protein E (CENP-E) inhibitor, is being developed under the strategic alliance by GSK; GSK began a Phase I clinical trial with GSK-923295 in 2007. In April 2008, Cytokinetics announced the selection of a potential drug candidate directed towards skeletal muscle contractility which may be developed as a potential treatment for skeletal muscle weakness associated with neuromuscular diseases or other conditions. All of these drug candidates and potential drug candidates have arisen from Cytokinetics' research activities and are directed towards the cytoskeleton. The cytoskeleton is a complex biological infrastructure that plays a fundamental role within every human cell. Additional information about Cytokinetics can be obtained at www.cytokinetics.com.

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, including the design, conduct and results of its Phase I/II clinical trial for SB-743921 and the potential significance of such results; the properties and potential clinical benefits of SB-743921 and Cytokinetics' other drug candidates and potential drug candidates; and the enabling capabilities of Cytokinetics' cytoskeletal focus. 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 approval, production and marketing of Cytokinetics' drug candidates that could slow or prevent clinical development, product approval or market acceptance, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trials results, patient enrollment for clinical trials may be difficult or take longer than anticipated, Cytokinetics' drug candidates may have unexpected adverse side effects or inadequate therapeutic efficacy, the U.S. Food and Drug Administration or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, and Cytokinetics may be unable to obtain and maintain patent or trade secret protection for its intellectual property; potential decisions by GSK to postpone or discontinue development efforts for GSK-923295 or not to exercise its options with respect to either or both of ispinesib and SB-743921; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing if necessary; standards of care may change rendering Cytokinetics' drug candidates and potential drug candidates obsolete or others may introduce products or alternative therapies for the treatment of indications Cytokinetics' drug candidates and potential drug candidates currently or potentially target; and risks and uncertainties relating to the timing and receipt of funds under Cytokinetics' collaborations. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.

Contacts:

Christopher S. Keenan (Investors and Media)
Director, Investor Relations
(650) 624-3000

SOURCE: Cytokinetics, Inc.