



Cytokinetics Announces Presentation of Preclinical Data for GSK-923295 at the 2007 AACR-NCI-EORTC International Conference

October 23, 2007 8:04 PM EDT

SOUTH SAN FRANCISCO, CA, Oct 23, 2007 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that two posters containing preclinical data relating to the mitotic kinesin centromere-associated protein E (CENP-E) and an inhibitor of CENP-E, GSK-923295, were presented today at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer in San Francisco. GSK-923295 is the subject of an ongoing first-time-in-humans Phase I clinical trial being conducted by GlaxoSmithKline (GSK) which is designed to evaluate the safety, tolerability and pharmacokinetics of GSK-923295 in patients with solid tumors.

Poster Presentations at AACR-NCI-EORTC International Conference:

The first poster presentation entitled, "Differential Response of Tumor Cell Lines to Inhibition of the Mitotic Checkpoint Regulator and Mitotic Kinesin, CENP-E," was presented on Tuesday, October 23, 2007 by lead author Penelope Chua of Cytokinetics. This poster presentation summarized the findings of a preclinical experiment designed to aid in identification of molecular determinants of sensitivity to GSK923295A, a novel and selective inhibitor of CENP-E motor domain enzymatic activity, currently in Phase I clinical trials. CENP-E is a kinesin motor protein functioning exclusively in mitosis to integrate mitotic spindle mechanics with mitotic checkpoint signaling. The authors concluded that certain cell lines, namely SK-BR-3, HCC1954 and EFM19, are sensitive to apoptosis following mitotic arrest with the inhibitor of CENP-E and that heterogeneity of response was observed. In addition, the poster detailed that cell death following mitotic arrest is not increased when slippage is induced by decreasing checkpoint strength, and furthermore, accumulation of p53 is correlated with mitotic arrest but does not correlate with sensitivity or resistance.

The second poster presentation entitled, "A Potent and Selective Inhibitor of the Mitotic Kinesin CENP-E (GSK923295A) Demonstrates a Novel Mechanism of Inhibiting Tumor Cell Proliferation and Shows Activity Against a Broad Panel of Human Tumor Cell Lines in vitro," was presented on Tuesday, October 23, 2007 by lead author David Sutton of GlaxoSmithKline. This poster presentation reported the findings of a preclinical study that evaluated the potential utility of GSK923295A as a cancer therapeutic. In this study, the compound was tested for anti-proliferative activity against 214 solid tumor cell lines and 85 hematological tumor cell lines. The authors concluded that GSK923295A, an inhibitor of human CENP-E, is active against a broad panel of both solid and hematological tumor lines in cell culture. In addition, the authors concluded that the activity of GSK923295A is not limited to any one tumor type. Furthermore, GSK923295A elicits a dose-dependent metaphase arrest in replicating tumor cells followed by an associated increase in apoptosis. Histological examination of treated cells revealed mitotic spindles with the majority of chromosomes aligned at the metaphase plate and a minority localized near the spindle poles, a phenotype consistent with CENP-E inhibition. With respect to selectivity for tumor cells, the separation between the sensitivities of bone marrow progenitor cells and many of the tumor cell lines suggests that anti-tumor activity with minimal myelosuppression might be achievable.

"These positive data provided the preclinical support for the recent initiation of the first-time-in-humans clinical trials of GSK-923295, an inhibitor of the mitotic kinesin, CENP-E," said David J. Morgans, Jr., Ph.D., Cytokinetics' Senior Vice President of Preclinical Research and Development. "Our translational research efforts are continuing to identify additional inhibitors of CENP-E, a promising target in the area of oncology. We look forward to data from GlaxoSmithKline's Phase I clinical trial in patients with solid tumors."

Development Status of GSK-923295

GSK-923295 is a small-molecule inhibitor of CENP-E and the third novel drug candidate to arise from Cytokinetics' broad strategic alliance with GSK. In August 2007, the company announced that GSK initiated a first-time-in-humans Phase I clinical trial of GSK-923295 in patients with solid tumors. This first Phase I clinical trial is an open-label, non-randomized, dose-finding trial designed to investigate the safety, tolerability and pharmacokinetics of GSK-923295 in patients with advanced solid tumors. As reported at the 2007 Annual Meeting of the American Association for Cancer Research (AACR), GSK-923295 demonstrated a broad spectrum of activity against a range of human tumor xenografts grown in nude mice, including models of colon, breast, ovarian, lung and other tumors.

Background on CENP-E

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. GSK-923295 is the first drug candidate to enter human clinical trials that specifically targets CENP-E. GSK began a Phase I clinical trial of GSK-923295 in 2007.

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 present in non-dividing cells. Cytokinetics believes that drugs that inhibit 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.

Background on Cytokinetics and GlaxoSmithKline Strategic Alliance

In June 2001, Cytokinetics and GSK entered into a broad strategic alliance to discover, develop and commercialize novel small molecule therapeutics targeting mitotic kinesins for applications in the treatment of cancer and other diseases. The strategic alliance has generated three drug candidates in clinical development, ispinesib and SB-743921, both inhibitors of kinesin spindle protein (KSP) and GSK-923295, an inhibitor of CENP-E. In June 2007, Cytokinetics announced a further one-year extension of the strategic alliance's research term, which began in June 2001, to continue activities focused towards translational research directed to CENP-E. Under a November 2006 amendment to its collaboration and license agreement with GSK, Cytokinetics assumed responsibility for the costs and activities associated with the continued development of ispinesib and SB-743921, subject to GSK's option to resume responsibility for some or all development and commercialization activities associated with each of these novel drug candidates, exercisable during a defined period. GSK-923295, now in a Phase I clinical trial in advanced cancers, is being developed under the strategic alliance by GSK. Cytokinetics will receive royalties from the sale of any products arising from the strategic alliance that GSK progresses to commercialization. For products that GSK progresses in development, Cytokinetics retains a product-by-product option to co-fund certain later-stage development activities, thereby potentially increasing its royalties and affording co-promotion rights in North America.

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' development efforts are directed to advancing multiple drug candidates through clinical trials to demonstrate proof-of-concept in humans, specifically in the areas of heart failure and cancer. Cytokinetics' cardiovascular disease program is focused to 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. plan to conduct research with activators of cardiac myosin in order to identify potential treatments for patients with heart failure. Amgen has obtained an option for the joint development and commercialization of CK-1827452 exercisable during a defined period, the ending of which is dependent on Cytokinetics' conduct of further clinical trials of CK-1827452. 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 believes that ispinesib has demonstrated clinical activity in Phase II monotherapy clinical trials in breast cancer, ovarian cancer and non-small cell lung cancer and plans to conduct additional clinical trials with ispinesib. Cytokinetics is also conducting a Phase I/II trial of SB-743921 in non-Hodgkin's lymphoma. GSK has obtained an option for the joint development and commercialization of ispinesib and SB-743921, exercisable during a defined period. Cytokinetics and GSK are conducting collaborative research activities 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 began a Phase I clinical trial with GSK-923295 in 2007. For products that GSK progresses in development, Cytokinetics retains a product-by-product option to co-fund certain later-stage development activities, thereby potentially increasing its royalties and affording co-promotion rights in North America. All of these drug candidates have arisen from Cytokinetics' research efforts and are directed towards 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 and cardiovascular disease. 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 Safe Harbor for forward-looking statements contained in the Act. Examples of such statements include, but are not limited to, statements relating to the expected conduct, scope and results of Cytokinetics' and its partners' planned research and development activities; Cytokinetics' receipt of royalties under its strategic alliance with GSK; the potential benefits of Cytokinetics' drug candidates and potential drug candidates; CENP-E as an oncology drug target; and the enabling capabilities of Cytokinetics' biological focus. Such statements are based on management's current expectations, but actual results may differ materially due to various factors. Such statements involve 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 delayed, 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; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing if necessary; standards of care may change 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: [

Scott R. Jordan (Media)
Director, Corporate Development
(650) 624-3000

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