



## **Cytokinetics Announces the Initiation of a Phase I Clinical Trial for GSK-923295**

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### **Third Drug Candidate to Enter Clinical Trials Under Strategic Alliance With GlaxoSmithKline; Initiation of Clinical Trial Triggers Milestone Payment to Cytokinetics**

SOUTH SAN FRANCISCO, CA, Aug 14, 2007 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that GlaxoSmithKline (GSK) has initiated a first-time-in-humans Phase I clinical trial of GSK-923295 in patients with solid tumors. GSK-923295 is a small-molecule inhibitor of centromere-associated protein E (CENP-E). 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. The initiation of this clinical trial triggers a milestone payment of \$1 million from GSK to Cytokinetics under the terms of the companies' strategic alliance established in June 2001.

This Phase I clinical trial is an open-label, non-randomized, dose-finding trial designed to investigate the safety, tolerability, pharmacokinetic and pharmacodynamic profile of GSK-923295 in patients with advanced solid tumors. GSK-923295 is the third novel drug candidate to arise from Cytokinetics' broad strategic alliance with GSK.

"We are pleased that GlaxoSmithKline has advanced GSK-923295 into clinical trials. Based on the broad anti-cancer activity we have seen in pre-clinical models, we are looking forward to evaluating the potential anti-cancer activity in humans for this novel drug candidate," stated Dr. Andrew A. Wolff, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer.

"The initiation of this Phase I clinical trial is further evidence of Cytokinetics' and GSK's commitment to build a solid scientific and clinical foundation for next-generation approaches to anti-cancer therapies," stated Robert I. Blum, Cytokinetics' President and CEO. "This drug candidate, along with others we are developing for the potential treatment of cancer and heart failure, demonstrates the productivity of Cytokinetics' research activities which have now generated four novel drug candidates moving towards proof-of-concept in multiple therapeutic indications."

#### **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.

#### **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 and GSK-923295. 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. The November 2006 amendment superseded a September 2005 amendment to the collaboration and license agreement, which specifically related to SB-743921.

#### **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, recently 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. 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. 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. Under a strategic alliance established in 2001, Cytokinetics and GlaxoSmithKline (GSK) are conducting research and development activities focused on the potential treatment of cancer. 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. 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](http://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 initiation and scope of Cytokinetics' and its partners' research and development programs, including statements regarding initiation of clinical trials; the potential benefits of Cytokinetics' drug candidates and potential drug candidates, including the benefits of mitotic kinesin inhibitors; 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 risks and uncertainties, including, but not limited to, potential decisions by GSK to postpone or discontinue development efforts for GSK-923295; 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, and Cytokinetics may be unable to obtain and 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 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.

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