



## **Cytokinetics Announces Non-Clinical Trial Data Presented at 2007 AACR Annual Meeting**

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### **Data Related to Ispinesib, GSK-923295 and Cytokinetics' Cell-Based Drug Discovery Program Support Advancement of Oncology Programs**

SOUTH SAN FRANCISCO, CA, Apr 18, 2007 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced the presentation of non-clinical data at the 2007 Annual Meeting of the American Association for Cancer Research (AACR) held in Los Angeles, CA from April 14-18, 2007. The presentations covered data evaluating ispinesib, a novel inhibitor of kinesin spindle protein (KSP), in models of multiple myeloma, data evaluating GSK-923295, a novel inhibitor of centrosome associated protein E (CENP-E) in both biochemical assays and in xenograft models and data from a separate, novel Cytokinetics cell-based drug discovery program.

"These presentations demonstrate the advancement of additional research oncology programs towards further development," stated David J. Morgans, Jr., Ph.D., Senior Vice President, Preclinical Research and Development. "This research not only identifies another potential development path for our leading oncology compound, ispinesib, and underscores enthusiasm for our potential drug candidate GSK-923295, expected to enter human clinical trials in 2007, but also points to future development opportunities that may arise from other ongoing drug discovery activities directed to cell cycle inhibition."

#### **Ispinesib**

The poster presentation entitled, "Kinesin Spindle Protein Inhibition for the Treatment of Multiple Myeloma," contained data arising from non-clinical studies designed to examine whether spindle disruption by inhibition of KSP with ispinesib may have therapeutic potential in the treatment of multiple myeloma. This presentation demonstrated that KSP inhibition with ispinesib was able to induce growth arrest and apoptosis in myeloma cells, and overcome resistance to both conventional drugs and novel agents, such as bortezomib. Moreover, the authors concluded that preferential activity against transformed plasma cells with sparing of normal bone marrow cells provides a rationale for translation of ispinesib into the clinic to combat relapsed/refractory multiple myeloma.

#### **GSK-923295**

The poster presentation entitled, "GSK-923295, a Potent and Selective CENP-E Inhibitor, Has Broad Spectrum Activity Against Human Tumor Xenografts in Nude Mice," contained data arising from non-clinical research on GSK-923295. In this presentation, the authors concluded that GSK-923295 is a potent and selective inhibitor of CENP-E. Furthermore, the data presented support the conclusion that GSK-923295 elicits dose-dependent increases in mitotic index in Colo205 tumor xenografts and an associated increase in apoptotic index, which is reflected histologically by an abundance of apoptotic bodies and mitotic spindles with the majority of chromosomes aligned at the metaphase plate, and a minority localized near the spindle poles, a phenotype identical to that which is observed in vitro. The authors also concluded that GSK-923295 has a broad spectrum of activity against a range of human tumor xenografts grown in nude mice.

The poster presentation entitled, "Detailed Biochemical Analysis of the CENP-E Inhibitor GSK-923295," contained data arising from biochemical analyses of GSK-923295. In this presentation, GSK-923295 was concluded to be an allosteric and specific inhibitor of human CENP-E and an inhibitor of the CENP-E microtubule stimulated ATPase. In addition, GSK-923295 was demonstrated to lock CENP-E onto microtubules and stabilize the ADP-Pi state of the microtubule-CENP-E complex. The authors concluded that GSK-923295 has a mode of inhibition consistent with the cellular response, namely cell cycle arrest with bipolar mitotic spindles and misaligned chromosomes, and has a unique mechanism of action compared to the KSP inhibitors, ispinesib and monastrol.

#### **Cytokinetics' Cell-Based Drug Discovery Program**

The poster presentation entitled, "Cell-based Discovery and Anti-tumor Activity of a Novel Mitotic Inhibitor," contained data arising from Cytokinetics' cell-based oncology drug discovery program. In this presentation, the authors identified a novel series of tumor-selective, anti-mitotic compounds which exhibited substantially less interphase activity than paclitaxel. The data presented demonstrated significant improvements in potency and drug properties of these compounds that were achieved without knowledge of the molecular target. Furthermore, the authors concluded that these compounds induced robust concentration-dependent cell cycle arrest in mitosis both in vitro and in vivo and promoted apoptosis.

#### **Clinical Trials for Ispinesib**

Ispinesib has been the subject of a broad Phase II clinical trials program under the sponsorship of GlaxoSmithKline (GSK) and is also being developed in collaboration with the National Cancer Institute (NCI). Under a November 2006 amendment to its collaboration and license agreement with GSK, Cytokinetics has assumed responsibility for the costs and activities associated with the continued development of the KSP inhibitors, 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. Cytokinetics plans to conduct, at its expense, a focused development program for ispinesib in breast cancer specifically designed to supplement the broad series of Phase I and Phase II clinical trials sponsored by GSK that have demonstrated clinical activity in the treatment of patients with metastatic breast cancer and that have shown an acceptable tolerability profile for ispinesib in combination with standard chemotherapeutics.

GSK has sponsored three Phase II clinical trials, one evaluating ispinesib as second- or third-line treatment for patients with locally advanced or metastatic breast cancer, one evaluating ispinesib as second-line treatment for patients with non-small cell lung cancer and one evaluating ispinesib as second-line treatment for patients with advanced ovarian cancer. Enrollment in all of these studies has been closed. To date, clinical activity for ispinesib has been observed in non-small cell lung cancer and breast cancer, with the more robust clinical activity observed in a Phase II clinical trial

evaluating ispinesib in the treatment of metastatic breast cancer patients that have failed treatment with taxanes and anthracyclines. GSK has informed Cytokinetics that final data is expected from the breast cancer clinical trial in the first half of 2007 and that a patient remains on study in the ovarian trial.

In addition, GSK has sponsored three dose-escalating Phase Ib clinical trials. Each of these clinical trials was designed to evaluate the safety, tolerability and pharmacokinetics of ispinesib in combination with a leading anti-cancer therapeutic, one in combination with carboplatin, the second in combination with capecitabine, and the third in combination with docetaxel. The clinical trial evaluating ispinesib in combination with capecitabine is ongoing.

The NCI has sponsored six additional Phase II clinical trials, one evaluating the potential efficacy of ispinesib in the second-line treatment of patients with colorectal cancer, one in the first-line treatment of patients with hepatocellular cancer, one in the first-line treatment of patients with melanoma, one in the first- or second-line treatment of patients with head and neck cancers, one in the second-line treatment of patients with hormone-refractory prostate cancer, and one in the second-line treatment of patients with renal cell cancer. Enrollment has been closed for all of these trials; patients remain on treatment in the renal cell cancer trial. Data are expected from the hepatocellular cancer, the prostate cancer, the melanoma, and the renal cell cancer trials in 2007. Data from other clinical trials have already been reported.

The NCI has completed patient treatment in a Phase I clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of ispinesib on an alternative dosing schedule in patients with advanced solid tumors that have failed to respond to all standard therapies; data from this trial have already been reported. The NCI is continuing patient enrollment in a Phase I clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of ispinesib on an alternative dosing schedule in patients with acute leukemia, chronic myelogenous leukemia or advanced myelodysplastic syndromes. Data from this trial are expected 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, appear to have no role in unrelated cellular functions. Cytokinetics believes that drugs that inhibit KSP and 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.

#### 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, 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 will 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 to 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 six 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 towards 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 is expected to begin clinical trials with GSK-923295 in 2007. All of these 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. 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, timing, conduct, scope and results of Cytokinetics' and its partners' research and development programs, including initiation of clinical trials, future presentations concerning Cytokinetics and its partners' research and development programs, anticipated dates of release of data from clinical trials; the incremental costs Cytokinetics expects to incur in connection with its ispinesib development program; and the potential benefits of Cytokinetics' drug candidates and potential drug candidates, including the benefits of mitotic kinesin inhibitors; and the enabling capabilities of our 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, that GSK or the NCI may decide to postpone or discontinue development efforts for GSK-923295 or ispinesib, respectively; that there may be difficulties or delays 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 not be able to obtain and maintain patent or trade secret protection for its intellectual property; that Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing if necessary; and that standards of care may change or others may introduce products or alternative therapies for the treatment of indications which Cytokinetics' drug candidates and potential drug candidates currently or potentially target. 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

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