



## **Cytokinetics Announces the Initiation of a Phase I/II Clinical Trial for Ispinesib in Metastatic Breast Cancer**

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### **Clinical Trial Designed to Evaluate Ispinesib as First-Line Monotherapy on an Alternate Dosing Schedule**

SOUTH SAN FRANCISCO, CA, Dec 31, 2007 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced the initiation of an open-label, non-randomized Phase I/II clinical trial designed to evaluate ispinesib monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced (Stage IIIB) or metastatic (Stage IV) breast cancer.

The Phase I portion of the trial is designed to determine the dose-limiting toxicity and maximum tolerated dose (MTD) of ispinesib monotherapy administered as a 1-hour intravenous infusion on days 1 and 15 of a 28-day cycle in female patients with locally advanced or metastatic adenocarcinoma of the breast who have not received prior chemotherapy. Once an MTD is determined, the clinical trial will move into Phase II of the trial, which is designed to assess the overall response rate to ispinesib of patients with measurable locally advanced or metastatic breast cancer who have not received prior chemotherapy, using the Response Evaluation Criteria In Solid Tumors (RECIST). Ispinesib will be administered as a 1-hour intravenous infusion on days 1 and 15 of a 28-day treatment cycle at the MTD determined in Phase I.

"We are pleased to initiate this clinical trial with ispinesib monotherapy in chemotherapy-naïve women with locally advanced or metastatic breast cancer," stated Dr. Andrew A. Wolff, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Given the anti-cancer activity we observed in a previous Phase II trial of ispinesib in women with locally advanced or metastatic breast cancer who were refractory to standard, approved therapy, we anticipate we may see an amplified signal of anti-cancer activity on this treatment schedule in this chemotherapy-naïve patient population."

#### **Ispinesib in Breast Cancer**

In June 2007, Cytokinetics reported final results of a Phase II clinical trial conducted by GlaxoSmithKline (GSK) designed to evaluate the safety and efficacy of ispinesib in the second- or third-line treatment of patients with locally advanced or metastatic breast cancer whose disease had recurred or progressed despite treatment with anthracyclines and taxanes. In this trial, patients received ispinesib monotherapy at 18 mg/m<sup>2</sup> as a 1-hour intravenous infusion every 21 days. The primary endpoint of the trial was objective response by RECIST. Partial responses, observed in 4 of 45 evaluable patients, were confirmed by independent radiology review and were seen in liver, lung and lymph node metastases. The duration of these responses, also independently reviewed, ranged from 7.1 weeks to 30.0 weeks. The median time to progression in the treated population was 5.9 weeks. The adverse events were manageable, predictable and consistent with those seen in the Phase I trials of ispinesib. The most common grade 3/4 adverse events observed in the 50 patients evaluable for safety were neutropenia (21 patients), febrile neutropenia (4 patients) and neutropenic sepsis (1 patient).

#### **Clinical Trials of Ispinesib**

Ispinesib has been the subject of a broad Phase II clinical trials program under the sponsorship of GSK and is also being developed in collaboration with the National Cancer Institute (NCI). GSK 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 with ispinesib has been observed in breast cancer as well as in ovarian and non-small cell lung cancer, with the most robust clinical activity observed in a Phase II clinical trial evaluating ispinesib in the treatment of patients with locally advanced or metastatic breast cancer that failed to respond or recurred after treatment with taxanes and anthracyclines.

In addition, GSK sponsored three dose-escalating Phase Ib clinical trials. Each of these 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 Phase Ib clinical trials of ispinesib in combination with carboplatin and docetaxel were completed in 2006 and demonstrated that ispinesib has an acceptable tolerability profile in combination with these standard chemotherapeutic agents. The clinical trial evaluating ispinesib in combination with capecitabine is closed to enrollment. Final data from this trial are expected in 2008.

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 the kinesin spindle protein (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 Phase I and Phase II clinical trials sponsored by GSK that demonstrated clinical activity in the treatment of patients with metastatic breast cancer and an acceptable tolerability profile for ispinesib in combination with capecitabine. The Phase I/II clinical trial announced today initiates this development program, the objective of which is to evaluate the possibility that ispinesib administered as monotherapy on days 1 and 15 of a 28-day cycle may demonstrate an amplified signal of clinical activity in chemotherapy-naïve breast cancer patients.

The NCI sponsored 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 and data have been reported for all of these trials.

The NCI 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 failed to respond to all standard therapies. Data from this trial have 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 relapsed or refractory acute leukemia, chronic myelogenous leukemia in blast crisis or advanced myelodysplastic syndromes. The NCI also continues to enroll patients in a Phase I clinical trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of ispinesib as monotherapy in pediatric patients with relapsed or refractory solid tumors.

#### 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 KSP and GSK-923295, an inhibitor of centromere associate protein E (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, subject to Cytokinetics' option to co-fund certain later-stage development activities and to co-promote any resulting approved drug in North America. GSK began a Phase I clinical trial 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 conduct, focus, scope and results of Cytokinetics' and its partners' planned research and development activities, including clinical trials; the potential benefits of ispinesib and Cytokinetics' other drug candidates and potential drug candidates; Cytokinetics' receipt of royalties under its collaboration with GSK; 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 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 ispinesib or Cytokinetics' other 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, ispinesib or Cytokinetics' other 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; 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 ispinesib or Cytokinetics' other 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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