Cytokinetics Announces Clinical and Preclinical Data Regarding Ispinesib Presented at the 31st Annual San Antonio Breast Cancer Symposium

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SOUTH SAN FRANCISCO, CA, Dec 12, 2008 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today that two posters, one summarizing interim Phase I clinical trial data evaluating ispinesib in the treatment of breast cancer and another containing preclinical data for ispinesib, were presented at the 31st Annual San Antonio Breast Cancer Symposium (SABCS) held on December 10-14, 2008. Ispinesib is a novel, small molecule inhibitor of kinesin spindle protein (KSP), a mitotic kinesin essential for proper cell division, being developed by Cytokinetics under a collaboration with GlaxoSmithKline.

A poster entitled, "A Phase I-II Trial of Ispinesib, a Kinesin Spindle Protein Inhibitor, Dosed Every Two Weeks in Patients with Locally Advanced or Metastatic Breast Cancer Previously Untreated with Chemotherapy for Metastatic Disease or Recurrence," was presented by Henry Gomez, M.D., Instituto Nacional de Enfermedades Neoplasicas, Lima, Peru. The primary objectives of the Phase I portion of this clinical trial are to determine the dose limiting toxicities (DLTs) and maximum tolerated dose and to assess the safety and tolerability of ispinesib administered as a 1-hour intravenous infusion on days 1 and 15 of a 28-day cycle. The secondary objectives are to characterize the pharmacokinetics of ispinesib on this schedule and to evaluate the potential effect of ispinesib on biomarkers of cell proliferation in patients with accessible tumors.

Interim results were provided for the first 16 patients enrolled at one of three dose levels of ispinesib (10 mg/m2, 12 mg/m2 and 14 mg/m2) and who had completed at least one cycle of treatment. At the time of data analysis, all sixteen patients were evaluable for safety and fifteen were evaluable for efficacy. Two of 7 patients treated at the 14 mg/m2 dose level had protocol-defined DLTs of transient Grade 3 increases in the liver enzymes ALT and AST following cycle 1, day 15 dosing. As a result of the DLTs at the 14 mg/m2 dose level, the 12 mg/m2 cohort was expanded to 6 patients; no DLTs were observed at this dose level. Because the 12 mg/m2 dose level was demonstrated to be tolerable, and because the authors concluded that the DLTs of Grade 3 ALT/AST increases at the 14 mg/m2 dose level had a questionable temporal relationship to ispinesib administration, plans are underway to further explore the 14 mg/m2 dose level. The most frequent adverse event was neutropenia, reported in 88% of patients, with 75% of patients experiencing Grade 3 or 4 neutropenia. Other than neutropenia and the Grade 3 ALT/AST increases described above, there were no other Grade 3 or 4 adverse events observed. No alopecia or neurotoxicity of any grade was reported. The best investigator-reported responses observed to date in the Phase I portion of this ongoing Phase I/II clinical trial were investigator-reported reductions of 30% or greater in the sum of the target lesion diameters, reported in 3 patients. Three patients had investigator-reported stable disease of 4 months or longer according to the Response Evaluation Criteria in Solid Tumors (RECIST).

Another poster entitled, "Ispinesib (SB-715992) a Kinesin Spindle Protein (KSP) Inhibitor has Single Agent Activity and Enhances the Efficacy of Standard-of-Care Therapies in Pre-clinical Models of Breast Cancer," was presented by James Purcell, Ph.D., Scientist, Cancer Biology and Therapeutics, of Cytokinetics, Inc. This presentation explored the anti-tumor activity of ispinesib in preclinical models of breast cancer, both as a single agent and in combination with therapies approved for the treatment of breast cancer. The authors concluded that ispinesib induced tumor regressions and tumor-free survival (90 days post-dosing) in ER positive, HER2 positive and triple negative models of breast cancer. In addition, they concluded that in the models studied, ispinesib can be combined with and enhances the anti-tumor activity of the standard-of-care breast cancer therapies trastuzumab, lapatinib, doxorubicin and capecitabine. In the triple negative models of breast cancer studied, ispinesib exhibited anti-tumor activity comparable to paclitaxel and ixabepilone.

Ispinesib in Breast Cancer

In September 2008, as part of a poster session at the ASCO Breast Cancer Symposium, Cytokinetics announced interim data from the Phase I portion of this ongoing Phase I/II clinical trial. At that time, the authors concluded that preliminary data suggest that ispinesib is well-tolerated when dosed on days 1 and 15 every 28 days at doses up to 12 mg/m2.

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 that trial, patients received ispinesib as monotherapy at 18 mg/m2 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 of 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, Cytokinetics believes clinical activity with ispinesib has been observed in breast, ovarian and non-small cell lung cancer, with the most robust clinical activity observed in GSK's 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 results of the Phase Ib clinical trial evaluating ispinesib in combination with capecitabine were announced in June 2008. The combination of ispinesib with capecitabine was found to have had an acceptable tolerability profile on the 21-day schedule investigated in the trial. The dose limiting toxicity in this combination regimen was consistent with the monotherapy toxicities of ispinesib (prolonged neutropenia) and capecitabine (rash). In this combination trial, the best response observed by RECIST was a partial response in a patient with advanced breast cancer and 11 patients had a response of stable disease.

Cytokinetics is conducting, 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 from which interim results were announced today is an integral part of 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-naive breast cancer patients.

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 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. 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-naive 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, future presentations concerning Cytokinetics' research and development programs, including the design, conduct and results of its Phase I/II clinical trial for ispinesib; the potential benefits of Cytokinetics' 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; 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 to not exercise its options 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; 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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