



Cytokinetics Announces Clinical Data Regarding Ispinesib in Combination With Capecitabine

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Drug Candidate Demonstrates Acceptable Safety and Tolerability in Phase Ib Trial

SOUTH SAN FRANCISCO, CA, Jun 30, 2008 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced today the results of a Phase Ib clinical trial designed to evaluate ispinesib in combination with capecitabine, an oral chemotherapy agent commonly used in the treatment of breast cancer. Ispinesib is a novel, small molecule inhibitor of kinesin spindle protein (KSP), a mitotic kinesin essential for proper cell division. Ispinesib, along with another KSP inhibitor, SB-743921 are chemically-distinct drug candidates that have arisen from a broad strategic collaboration between Cytokinetics and GlaxoSmithKline (GSK) to discover, develop and commercialize novel small molecule therapeutics targeting human mitotic kinesins for applications in the treatment of cancer and other diseases.

This Phase Ib clinical trial, sponsored by GSK, was an open-label, dose-escalation study of ispinesib in combination with capecitabine on an every 21-day schedule in subjects with advanced solid tumors. Its primary objectives were to assess the safety and tolerability and to determine the optimally tolerated regimen (OTR) of ispinesib when administered as a 1-hour infusion on Day 1 in combination with daily administration of capecitabine given on Days 1 through 14 of the 21-day cycle. The secondary objective was to assess the clinical activity of this combination in patients with advanced solid tumors. Although a single dose regimen was not formally confirmed as the OTR, ispinesib administered at 18 mg/m², its maximum tolerated dose as monotherapy, was well-tolerated in combination with therapeutic doses of capecitabine [0] at daily doses of 2000 mg/m² and 2500 mg/m². The investigators in this clinical trial concluded that the combination of ispinesib with capecitabine 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 trial, the best response observed among the 24 patients treated was a partial response by Response Evaluation Criteria In Solid Tumors (RECIST) in a patient with advanced breast cancer. In addition, 11 patients had a response of stable disease by RECIST.

These encouraging data support the ongoing development plans for ispinesib, stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. In particular, given that capecitabine is a commonly used chemotherapeutic for treatment of patients with advanced breast cancer, the results of this combination study may be promising for future development of ispinesib in patients with breast cancer.

About Ispinesib

In June 2007, Cytokinetics reported final results of a Phase II clinical trial conducted by 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 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).

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 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 has completed 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.

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 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. Cytokinetics is currently conducting a Phase I/II clinical of ispinesib designed 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.

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-associated protein E (CENP-E). In June 2008, 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. The November 2006 amendment superseded a September 2005 amendment to the collaboration and license agreement, which specifically related to SB-743921. 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 providing Cytokinetics an opportunity to increase its potential royalties and obtain co-promotion rights for the applicable products 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 activities are primarily directed to advancing multiple drug candidates through clinical trials with the objective of determining the intended pharmacodynamic effect or effects in two principal diseases: 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. 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 believes clinical activity for ispinesib has been observed in Phase II monotherapy clinical trials in breast cancer, ovarian cancer and non-small cell lung cancer and recently initiated an additional Phase I/II clinical trial of ispinesib as monotherapy as a first-line treatment in chemotherapy-naïve patients with locally advanced or metastatic breast cancer on a more dose-dense schedule than previously studied. Cytokinetics is also conducting a Phase I/II trial of SB-743921 on a similar more dose-dense schedule in non-Hodgkin and Hodgkin lymphomas. GSK has obtained an option for the joint development and commercialization of ispinesib and SB-743921. 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. 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. 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 and other diseases. 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 Cytokinetics' and its partners' research and development activities, including the conduct, design, focus, scope and results of clinical trials; 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 or production of Cytokinetics' drug candidates that could slow or prevent clinical development, product approval, 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 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 or maintain patent or trade secret protection for its intellectual property; GSK may decide to postpone or discontinue development activities for GSK-923295. Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products, standards of care may change, others may introduce products or alternative therapies for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target, and risks and uncertainties relating to the timing and receipt of payments from our partners, including milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. 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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