

# **Cytokinetics Reports Additional Clinical Trials Data for Ispinesib**

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# **Results Reported From Three NCI-Sponsored Clinical Trials**

SOUTH SAN FRANCISCO, CA, Jun 28, 2007 (MARKET WIRE via COMTEX News Network) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced results from the analyses of three Phase II clinical trials of ispinesib administered as monotherapy, one in patients with hepatocellular cancer, one in patients with melanoma, and one in patients with hormone-refractory prostate cancer. Ispinesib is a novel small molecule inhibitor of kinesin spindle protein (KSP), a mitotic kinesin essential for proper cell division. Ispinesib has 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. All three clinical trials were sponsored by the National Cancer Institute (NCI).

A Phase II clinical trial designed to evaluate the safety and efficacy of ispinesib in the treatment of patients with locally advanced, recurrent or metastatic hepatocellular cancer was recently completed. In Stage 1 of this two-stage clinical trial, 15 patients received ispinesib as monotherapy at 18 mg/m2 as a 1-hour intravenous infusion every 21 days. The trial's primary endpoint was objective response as determined using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria. This trial was designed to require at least 1 confirmed partial or complete response out of 15 evaluable patients in Stage 1 in order to proceed to Stage 2. The best overall response was stable disease seen in 7 of the 15 patients treated. In this clinical trial, ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The toxicity profile was consistent with other previously reported Phase II clinical trials of ispinesib. A manuscript is being prepared.

A Phase II clinical trial designed to evaluate the safety and efficacy of ispinesib in the treatment of patients with chemotherapy-naive recurrent or metastatic malignant melanoma was recently completed. In Stage 1 of this two-stage clinical trial, 17 patients received ispinesib as monotherapy at 18 mg/m2 as a 1-hour intravenous infusion every 21 days. The trial's primary endpoint was objective response as determined using the RECIST criteria. This trial was designed to require at least 1 confirmed partial response in 15 patients in Stage 1 in order to proceed to Stage 2. The best overall response was stable disease seen in 6 of 17 patients treated. In this clinical trial, ispinesib did not satisfy the criteria for advancement to the second stage and therefore recruitment to Stage 2 was not opened. The toxicity profile was consistent with other previously reported Phase II clinical trials of ispinesib. A manuscript is being prepared.

A Phase II clinical trial designed to evaluate the safety and efficacy of ispinesib for the treatment of hormone refractory prostate cancer who had failed taxane-based chemotherapy was recently completed. In Stage 1 of this two-stage clinical trial, 21 patients received ispinesib as monotherapy at 18 mg/m2 as a 1-hour intravenous infusion every 21 days. The trial's primary endpoint was objective response as determined using the RECIST criteria and a prostate-specific antigen (PSA) response of a greater than 50% decline confirmed 3 weeks later. This trial was designed to require a minimum of 1 PSA response in the first 20 evaluable patients in Stage 1 in order to proceed to Stage 2. No patient met the criteria for a PSA response and the median time to PSA or clinical progression was 9 weeks. In this clinical trial, ispinesib did not satisfy the criteria for advancement to the next stage in the clinical trial. The toxicity profile was consistent with other previously reported Phase II clinical trials of ispinesib. A manuscript is being prepared.

"These three Phase II clinical trials sponsored by NCI are components of a clinical trials program designed to identify signals of clinical activity of ispinesib across multiple tumor types," stated Dr. Andrew A. Wolff, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Although these three trials did not meet the protocol-specified criteria for progression, we are encouraged by the anti-cancer activity of ispinesib observed to date in three other Phase II trials in breast, ovarian and non-small cell lung cancers. Based on these data, we plan to move forward in further clinical development of ispinesib with a focused approach to the potential treatment of breast cancer with ispinesib."

## Clinical Trials of 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 NCI. 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 trials has been closed. To date, clinical activity with ispinesib has been observed in breast cancer, in non-small cell lung cancer, and ovarian 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. In this clinical trial, The best overall responses observed with ispinesib were partial responses in 4 of 45 evaluable patients as measured by the RECIST criteria. Responses were confirmed by independent radiology review and were seen in liver, lung and lymph node metastases. The duration of response, 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 were neutropenia, febrile neutropenia and neutropenic sepsis.

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 closed to enrollment. Final data from this trial are expected in 2007.

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.

The NCI has sponsored six additional Phase II clinical trials, evaluating the potential efficacy of ispinesib in an array of different tumor types. Enrollment has been closed for all of these trials; patients remain on treatment in the renal cell cancer trial. Data from the other 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 relapsed or refractory acute leukemia, chronic myelogenous leukemia in blast crisis, 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 other 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 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 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 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 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.

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; anticipated dates of release of data from 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, 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.

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