



Cytokinetics Reports Data for Ispinesib in Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma

October 2, 2006 4:00 AM EDT

South San Francisco, CA, October 2, 2006 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced results from a planned interim analysis following Stage 1 of a two-stage Phase II clinical trial of *ispinesib* administered as monotherapy in the treatment of patients with recurrent and/or metastatic head and neck squamous cell carcinoma (RMHNSC). This clinical trial was conducted by the National Cancer Institute (NCI) under a collaboration with GlaxoSmithKline (GSK). A presentation entitled, "A Phase II Study of *ispinesib* in Patients with Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma" was made at the European Society of Medical Oncology in Istanbul, Turkey on Monday, October 2, 2006, by Patricia Tang, M.D. of the Princess Margaret Hospital Phase II Consortium, Toronto, Canada.

This Phase II clinical trial was designed to evaluate the safety and efficacy of *ispinesib* administered at 18 mg/m² as an intravenous one hour infusion once every 21 days in patients with RMHNSC, who had received no more than one prior chemotherapy regimen. This two-stage clinical trial was designed to require a minimum of 1 confirmed partial or complete response out of 19 evaluable patients in Stage 1 in order to proceed to Stage 2. The trial's primary endpoint was response rate as determined using RECIST criteria. A total of 21 patients were enrolled; one patient did not receive *ispinesib* due to disease progression prior to treatment, and another was evaluable for safety but not efficacy.

At the interim analysis after Stage 1 of this clinical trial, *ispinesib* in patients with RMHNSC at this dosing level did not satisfy the criteria for advancement to Stage 2. The best overall response to date in this clinical trial was disease stabilization, which was observed in 5 of the 19 patients evaluable for efficacy at cycle 2. Overall, median time to disease progression was 5.9 (95% CI 5.4-10.0) weeks. The safety and pharmacokinetics of *ispinesib* in this clinical trial were evaluated in 20 of the patients enrolled in the trial. The most frequently observed adverse events of any grade that were viewed by the investigator to be possibly related to *ispinesib* (percent of patients treated) were leukopenia (65%) and neutropenia (65%). Other common adverse events included nausea (35%), hyponatremia (30%), fatigue (25%), lymphopenia (25%), anemia (20%), injection site reaction (15%), vomiting (15%), and bone pain (5%). The most common grade 3 or greater adverse event was neutropenia, occurring in 55% of patients treated. Two patients died on study. One death in a patient with a non-neutropenic infection (grade 3) was attributed to progressive disease, the other, in a patient with four days of grade 3-4 neutropenia, was attributed to pneumonia.

Background on KSP 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 the peripheral nervous system. Neuropathies 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.

The strategic alliance established between Cytokinetics and GSK in 2001 has yielded two novel drug candidates that inhibit kinesin spindle protein (KSP), *ispinesib* (SB-715992) and SB-743921. *ispinesib* and SB-743921 are structurally distinct small molecule compounds that modulate cell proliferation and promote cancer cell death by specifically inhibiting KSP. KSP is a mitotic kinesin that is essential for cell proliferation, a process which, when unregulated, results in tumor growth. Mitotic kinesins are essential to mitosis, and, unlike tubulin, appear to have no role in unrelated cellular functions. We believe that drugs that inhibit KSP 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, thus potentially avoiding many of the toxicities commonly experienced by patients treated with existing anti-mitotic drugs.

About *ispinesib*

ispinesib is a novel small molecule inhibitor of KSP, a mitotic kinesin protein essential for proper cell division. *ispinesib* is the first drug candidate in clinical development that has arisen from a broad strategic collaboration between Cytokinetics and GSK to discover, develop and commercialize novel small molecule therapeutics targeting human mitotic kinesins for applications in the treatment of cancer and other diseases. GSK is conducting a broad clinical trials program for *ispinesib* designed to study this drug candidate in multiple tumor types, combination regimens and dosing schedules. GSK is currently evaluating *ispinesib* in two Phase II clinical trials being conducted in patients with each of ovarian and breast cancers and two Phase Ib clinical trials designed to evaluate *ispinesib* in combination with each of carboplatin and capecitabine.

In addition to the ongoing studies being conducted by GSK and the RMHNSC study reported today, the NCI is conducting four other Phase II clinical trials evaluating *ispinesib* in other tumor types, including hepatocellular, prostate, and renal cell cancers and in melanoma. The NCI is also conducting two other Phase I clinical trials evaluating a new schedule of *ispinesib*, one in leukemia and another in advanced solid tumors, and is expected to initiate a Phase I clinical trial evaluating *ispinesib* as monotherapy in pediatric patients with relapsed or refractory solid tumors in the second half of 2006.

About SB-743921

SB-743921, Cytokinetics' second KSP inhibitor to enter clinical trials under the strategic alliance with GSK, is structurally distinct from *ispinesib*, Cytokinetics' most advanced drug candidate. In September 2005, Cytokinetics and GSK announced an amendment to their original collaboration agreement to support further expansion of the development activities for SB-743921. Under the terms of the amendment, Cytokinetics is responsible for leading and funding development activities to explore the potential application of SB-743921 for the treatment of non-Hodgkin's lymphoma (NHL), Hodgkin's disease and multiple myeloma, subject to GSK's option to resume responsibility for development and commercialization activities for SB-743921 for these indications during a defined period. Cytokinetics' development activities will be conducted in parallel with GSK's development activities for SB-743921 in other indications and for *ispinesib*. In April 2006, Cytokinetics announced the initiation of a Phase I/II clinical trial of SB-743921 in patients with NHL, in connection with an expanded development program for SB-743921. This Phase I/II clinical trial is an open-label, non-randomized study to investigate the safety, tolerability, pharmacokinetic, and pharmacodynamic profile of SB-743921, administered as a one-hour infusion on days 1 and 15 of a 28-day schedule, and to assess the potential efficacy of the maximum tolerated dose of SB-743921 administered on this schedule in patients with NHL.

About Cytokinetics

Cytokinetics is a biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule drugs that specifically target 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, cardiovascular disease and other diseases. Under a strategic alliance established in 2001, Cytokinetics and GSK are collaborating to develop and commercialize small molecule therapeutics targeting human mitotic kinesins for applications in the treatment of cancer and other diseases. *ispinesib* (SB-715992), SB-743921 and GSK-923295 are being developed under the strategic alliance with GSK. GSK is conducting Phase II and Ib clinical trials for *ispinesib* and Cytokinetics is conducting a Phase I/II trial of SB-743921 in non-Hodgkin's lymphoma. Cytokinetics' unpartnered cardiovascular disease program is the second program to leverage the company's expertise in cytoskeletal pharmacology. Cytokinetics recently completed a Phase I clinical trial with CK-1827452, a novel small molecule cardiac myosin activator, for the intravenous treatment of heart failure and also is advancing CK-1827452 as a potential drug candidate for the treatment of chronic heart failure via oral administration. Additional information about Cytokinetics can be obtained at <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 Cytokinetics and its partners' clinical research and development programs, including expected future clinical trials, the potential benefits of Cytokinetics' drug candidates and potential drug candidates and the enabling capabilities of Cytokinetics' proprietary technologies. Such statements are based on management's current expectations, but actual results may differ materially due to various factors. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to decisions by the NCI to postpone or discontinue development efforts for one or more compounds, difficulties or delays in patient enrollment for clinical trials, unexpected adverse side effects or inadequate therapeutic efficacy of Cytokinetics' drug candidates and other potential difficulties or delays in development, testing, regulatory approval, production and marketing of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval (including the risks relating to uncertainty of patent protection for Cytokinetics' intellectual property or trade secrets and Cytokinetics' ability to obtain additional financing if necessary and unanticipated research and development and other costs), the conduct of activities and continued funding under Cytokinetics' collaborations and the implementation and maintenance of procedures, policies, resources and infrastructure relating to compliance with new or changing laws, regulations and practices. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.