Cytokinetics Reports Data for Ispinesib (SB-715992) in Platinum-Sensitive Non-Small Cell Lung Cancer

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Cytokinetics Reports Data for Ispinesib (SB-715992) in Platinum-Sensitive Non-Small Cell Lung Cancer - Drug Candidate Does Not Demonstrate Sufficient Anti-Tumor Activity to Proceed to Stage 2 in this Phase II Clinical Trial Drug Candidate Demonstrates Disease Stabilization in 50% of Patients

South San Francisco, CA, March 30, 2006 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced results from a planned interim analysis of a Phase II clinical trial of ispinesib administered as monotherapy in the treatment of patients with platinum-sensitive non-small cell lung cancer. This clinical trial is being conducted by Cytokinetics' alliance partner, GlaxoSmithKline (GSK).

In a Phase II clinical trial designed to evaluate the safety and efficacy of ispinesib in the second-line treatment of patients with either platinum-sensitive or platinum-refractory non-small cell lung cancer, ispinesib has not satisfied the criteria for advancement to the next stage in the platinum-sensitive treatment arm. This clinical trial was designed to require a minimum of 1 confirmed partial or complete response out of 20 evaluable patients in a treatment arm to proceed to Stage 2 in that treatment arm. The trial's primary endpoint is response rate as determined using RECIST criteria. The best overall responses to date in the platinum-sensitive treatment arm of this clinical trial have been disease stabilization observed in 10 of 20 evaluable patients. Overall, median time to disease progression was 6 weeks; in the 10 patients whose best response was stable disease, median time to progression was 17 weeks.

The platinum-refractory treatment arm of this clinical trial was completed in 2005; Cytokinetics announced in September of 2005 that the platinum-refractory treatment arm also did not satisfy the criteria for advancement to the next stage of evaluation. In that treatment arm, disease stabilization was observed in 5 of 20 evaluable patients. Overall, median time to disease progression was 6 weeks; in the 5 patients whose best response was stable disease, median time to progression was 12 weeks.

“While we are encouraged by both the frequency and duration of disease stabilization observed in the platinum-sensitive treatment arm of this trial, we are disappointed that we did not achieve the objective response rate required by the protocol to continue enrollment in Stage 2,” stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. “We are awaiting data from ongoing Phase Ib combination trials involving ispinesib. With the demonstrated frequency and duration of disease stabilization observed in this patient population and ispinesib's tolerability profile, we plan to consider a potential role that this drug candidate could play in the treatment of patients with non-small cell lung cancer potentially in combination with other chemotherapeutics.”

The safety and pharmacokinetics of ispinesib in the platinum-sensitive treatment arm of this clinical trial appears comparable to that observed from its Phase I clinical trial experience at equivalent doses and from the platinum-refactory treatment arm in this clinical trial. The most significant side effect observed was Grade 4 neutropenia in 10 patients. With the exception of neutropenia (11 patients), febrile neutropenia (3 patient) and fatigue (2 patients), no other significant side effects of higher than Grade 2 were observed.

“We have now evaluated ispinesib in over one hundred patients with cancer and its administration seems to be very well-tolerated, with the only significant side effect being Grade 4 neutropenia. We have not observed side effects commonly associated with currently approved anti-mitotics, such as neurotoxicity and alopecia, that may limit dosing patients with advanced disease,” added James Sabry, M.D., Ph.D., Chief Executive Officer. “We have previously observed clinical activity of ispinesib in patients with locally advanced or metastatic breast cancer. We look forward to further data from the broad clinical trials program currently underway with ispinesib, which is designed to evaluate the clinical potential of this novel drug candidate in multiple tumor types, dosing schedules and treatment combinations and which may inform next steps.”

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 between Cytokinetics and GSK has yielded two novel drug candidates, 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 kinesin spindle protein (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, avoiding many of the toxicities commonly experienced by patients treated with existing anti-mitotic drugs.

Clinical Trials Status for Ispinesib

Ispinesib is the subject of a broad clinical trials program under the sponsorship of GSK and the National Cancer Institute (NCI). GSK is currently conducting two Phase II clinical trials, one evaluating ispinesib as second- or third-line treatment for patients with locally advanced or metastatic breast cancer and one evaluating ispinesib as second-line treatment for patients with advanced ovarian cancer. Data were presented at the 2005 San Antonio Breast Cancer Symposium demonstrating sufficient anti-tumor activity with ispinesib to proceed to Stage 2 in an ongoing Phase II clinical trial evaluating ispinesib as monotherapy in patients with locally advanced or metastatic breast cancer. The best overall responses observed in that trial have been partial responses observed in 3 of 33 patients. In addition, GSK is continuing three dose-escalating Phase Ib clinical trials. Each of these clinical trials is 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 NCI, in collaboration with GSK, continues to sponsor five additional Phase II clinical trials evaluating the potential efficacy of ispinesib in the second-line

treatment of patients with colorectal cancer, in the first-line treatment of patients with hepatocellular cancer, in the first-line treatment of patients with melanoma, in the first-line or second-line treatment of patients with head and neck cancers, and in the second-line treatment of patients with hormone-refractory prostate cancer. In addition, the NCI plans to initiate an additional Phase II clinical trial to evaluate the potential efficacy of ispinesib as second-line treatment of patients with renal cell cancer. The NCI also continues patient enrollment in two additional Phase I clinical trials designed to evaluate the safety, tolerability and pharmacokinetics of ispinesib on an alternative dosing schedule. One clinical trial is enrolling patients with advanced solid tumors that have failed to respond to all standard therapies and the other clinical trial is enrolling patients with acute leukemia, chronic myelogenous leukemia or advanced myelodysplastic syndromes.

Clinical Trials Status for SB-743921

SB-743921 entered a Phase I clinical trial conducted by GSK in the United States in May 2004 to evaluate its tolerability and pharmacokinetics in patients with advanced cancer. Data relating to SB-743921 were presented at the 2005 Annual Meeting of the American Society of Clinical Oncology in May 2005. The data presented were from 20 patients that collectively had a variety of advanced solid tumors and received doses of SB-743921 intravenously once every 21 days. SB-743921 appears to have an acceptable tolerability profile for patients suffering from advanced solid tumors. The dose-limiting toxicities observed to date are prolonged neutropenia, febrile neutropenia (with or without infection), elevated transaminases, hyperbilirubinemia and hyponatremia. Notably, neurotoxicities, mucositis, thrombocytopenia, alopecia and nausea/vomiting requiring pre-medication have not been observed to date. In September of 2005, Cytokinetics announced the amendment of the company's strategic alliance with GSK, which will provide Cytokinetics an expanded role in clinical research and development for SB-743921, a novel, small molecule inhibitor of kinesin spindle protein (KSP). Under the terms of the amendment, Cytokinetics will lead and fund development activities to explore the potential application of SB-743921 for the treatment of non-Hodgkin's lymphoma, Hodgkin's lymphoma and multiple myeloma, subject to the option for GSK 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 conduct of development activities for SB-743921 in other indications and for ispinesib (SB-715992).

About Cytokinetics

Cytokinetics is a leading 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. Cytokinetics has developed a cell biology driven approach and proprietary technologies to evaluate the function of many interacting proteins in the complex environment of the intact human cell. Cytokinetics employs the PUMA™ system and Cytometrix™ technologies to enable early identification and automated prioritization of compounds that are highly selective for their intended protein targets without other cellular effects, and may therefore be less likely to give rise to clinical side effects. Cytokinetics and GlaxoSmithKline (GSK) have entered into a strategic alliance to discover, develop and commercialize small molecule therapeutics targeting human mitotic kinesins for applications in the treatment of cancer and other diseases. GSK is conducting Phase II and Ib clinical trials for ispinesib (SB-715992) and a Phase I clinical trial for SB-743921. Ispinesib, SB-743921 and GSK-923295 are being developed under the strategic alliance with GSK. Cytokinetics' unpartnered heart failure program is the second program to leverage the company's expertise in cytoskeletal pharmacology. Cytokinetics recently initiated a Phase I clinical trial with CK-1827452, a novel small molecule cardiac myosin activator, for the intravenous treatment of heart failure and also selected 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 www.cytokinetics.com.

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