



## **Cytokinetics Announces Initiation of Phase II Clinical Trial in Renal Cell Cancer and Phase I Clinical Trial in Pediatric Solid Tumors**

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### **Cytokinetics Announces Initiation of Phase II Clinical Trial in Renal Cell Cancer and Phase I Clinical Trial in Pediatric Solid Tumors - Cytokinetics Provides Update on Ispinesib Clinical Trials Progress**

South San Francisco, CA, December 20, 2006 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced today that the National Cancer Institute (NCI) has initiated a Phase II clinical trial to evaluate the potential efficacy of the kinesin spindle protein (KSP) inhibitor, ispinesib (SB-715992), as a second-line treatment for patients with renal cell cancer and a Phase I clinical trial to evaluate ispinesib as a monotherapy in pediatric patients with relapsed or refractory solid tumors. The NCI is sponsoring these trials as a part of a clinical development program to evaluate the safety and efficacy of ispinesib as monotherapy in multiple tumor types and in combination with other standard chemotherapeutics.

The Phase II clinical trial in renal cell patients is an open-label study to investigate the safety and efficacy of ispinesib, administered at 7mg/m<sup>2</sup> as a one-hour infusion on days 1, 8 and 15 of a 28-day schedule. In this Phase II clinical trial, between 18 and 35 renal cell patients are planned to be treated. The clinical trial's primary endpoint is response rate as determined by the Response Evaluation Criteria in Solid Tumors (RECIST).

The Phase I clinical trial in pediatric patients with relapsed or refractory solid tumors is a dose-finding clinical trial designed to investigate the safety, tolerability, pharmacokinetics and pharmacodynamic profile of ispinesib administered as a one-hour infusion on days 1, 8 and 15 of a 28-day schedule in this patient population. In this Phase I clinical trial, 30 pediatric patients with relapsed or refractory solid tumors are planned to be treated.

#### **Clinical Trials for Ispinesib**

Ispinesib has been the subject of a broad clinical trials program under the sponsorship of GlaxoSmithKline (GSK) and is also being developed in collaboration with the NCI. In November 2006, Cytokinetics amended the company's collaboration and license agreement with GSK. Under this amendment, Cytokinetics will assume responsibility for the costs and activities of 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 a focused development program for ispinesib 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 and lung cancers and that have shown an acceptable tolerability profile for ispinesib in combination with standard chemotherapeutics. This development program will focus to breast cancer and Cytokinetics expects to incur approximately \$4-7 million of incremental costs in 2007 related to assuming additional clinical development responsibilities under the amendment to the collaboration agreement with GSK.

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 studies has been closed. GSK has informed Cytokinetics that final data is expected from the breast cancer clinical trial in the first half of 2007 and that a patient remains on study in the ovarian trial. Cytokinetics will provide guidance in 2007 regarding the expected timing of data from the ovarian clinical trial.

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 ongoing.

The NCI has sponsored 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. Enrollment has been closed for all of these clinical trials. Data are expected from the hepatocellular cancer clinical trial, the prostate cancer clinical trial and the melanoma clinical trial in the first half of 2007. Data arising from other clinical trials have already 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 advanced solid tumors that have failed to respond to all standard therapies. 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 acute leukemia, chronic myelogenous leukemia or advanced myelodysplastic syndromes. Data from both of these trials 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 proteins essential to mitosis, and, unlike tubulin, appear to have no role in unrelated cellular functions. Cytokinetics believes that drugs that inhibit KSP and centromere-associated protein E (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.

#### **Background on Cytokinetics and GSK Agreement**

In June 2001, Cytokinetics and GSK announced that the companies had entered into a collaboration agreement for 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 two drug candidates in clinical development, ispinesib and SB-743921, and one potential drug candidate in preclinical development, GSK-923295. In September 2005, Cytokinetics and GSK amended the collaboration agreement to provide Cytokinetics an expanded role in the clinical research and development of SB-743921; the September 2005 amendment has been superseded by the November 2006 amendment. In June 2006, Cytokinetics announced the extension of the research term of this strategic alliance for an additional year, beyond the original minimum of five years, to continue activities focused towards translational research directed to CENP-E.

Under the terms of the November 2006 amendment to the collaboration agreement, Cytokinetics, at its expense, will assume responsibility for the continued research, development and commercialization of inhibitors of KSP, including ispinesib and SB-743921, and other mitotic kinesins, other than CENP-E which is the focus of translational research activities being conducted by GSK and Cytokinetics and development activities being conducted by GSK. The ongoing activities for CENP-E are coordinated under an agreed joint research program during an extended research term under the June 2006 amendment to the collaboration agreement. Under the November 2006 amendment, Cytokinetics' development of ispinesib and SB-743921 is subject to GSK's option to resume responsibility for the development and commercialization of either or both drug candidates during a defined period and in accordance with agreed terms. If GSK exercises its option for a drug candidate, it will pay Cytokinetics an option fee equal to the costs Cytokinetics independently incurred for that drug candidate, plus a premium intended to compensate Cytokinetics for the cost of capital associated with such costs, subject to an agreed limit for such costs and premium. Upon GSK exercising its option for a drug candidate, Cytokinetics may receive additional pre-commercialization milestone payments with respect to such drug candidate and increased royalties on net sales of any resulting product, in each case, beyond those contemplated under the original agreement. If GSK does not exercise its option for a drug candidate, Cytokinetics will be obligated to pay royalties to GSK on the sales of any resulting products. The November 2006 amendment supersedes a previous amendment to the collaboration agreement dated September 2005, which specifically related to SB-743921.

Cytokinetics is considering a development plan for the further evaluation of ispinesib for the treatment of breast cancer and may further explore the combination treatment approach of ispinesib with capecitabine. This strategy is informed by evidence of clinical activity observed in a monotherapy clinical trial of ispinesib in the second-line or third-line treatment of advanced breast cancer patients and in a combination therapy clinical trial of ispinesib and capecitabine. In addition, Cytokinetics is currently conducting a Phase I/II clinical trial of SB-743921 in patients with non-Hodgkin's lymphoma (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 conducting research and development activities focused towards the potential treatment of cancer and other indications. Cytokinetics and GSK are continuing collaborative research focused to translational research directed to the mitotic kinesin CENP-E. GSK-923295, a CENP-E inhibitor, is being developed under the strategic alliance by GSK; GSK expects to begin clinical trials with GSK-923295 in 2007. Cytokinetics is responsible for the development of ispinesib and SB-743921, each a novel inhibitor of the mitotic kinesin KSP. Ispinesib has been the subject of a broad clinical trials program comprising 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 NHL. 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 and an oral bioavailability study with CK-1827452, a novel small molecule cardiac myosin activator, and is advancing CK-1827452 in both intravenous and oral formulations for the treatment of heart failure. 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 the expected initiation, timing, scope and targeted indications of clinical trials within Cytokinetics' and its partners' clinical development and research programs, the potential benefits of Cytokinetics' drug candidates and potential drug candidates 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 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 research and/or development efforts for ispinesib or by GSK to postpone or discontinue research and/or development efforts for CENP-E, 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, product approval or market acceptance (including the risks relating to uncertainty of patent or trade secret protection for Cytokinetics' intellectual property, Cytokinetics' ability to obtain additional financing if necessary and unanticipated research and development and other costs), and changing standards of care and the introduction by others of products or alternative therapies for the treatment of indications currently or potentially targeted by Cytokinetics' drug candidates and potential drug candidates. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.