



## **Synta Pharmaceuticals Presents Preliminary Data at ASCO for STA-4783 in Patients with Non-Small Cell Lung Cancer and Soft Tissue Sarcoma**

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STA-4783's Novel Mechanism of Action in Combination with Leading Cancer Therapy Suggests Encouraging Response and Non-Progression Rates

Orlando, Fla. - May 17, 2005 - Synta Pharmaceuticals today announced presentation of preliminary data from two of its ongoing Phase 2 trials of its lead oncology compound STA-4783 administered in combination with paclitaxel in patients with non-small cell lung cancer (NSCLC) and soft tissue sarcoma. The reported data from the trials are from the first stage, open-label portion of these two-stage trials, and in both cases supported advancement to the second stage of the trial. These preliminary Phase 2 data, together with the results from Synta's Phase 1 trial of STA-4783 in patients with a broad range of cancer types, were presented at the Annual Meeting of the American Society of Clinical Oncology (ASCO) held May 13-17, 2005 in Orlando, Fla.

STA-4783 has a novel, dual mechanism of action. STA-4783 induces the expression of heat shock protein 70 (Hsp70) on the surface of tumor cells, which flags the cells for destruction and elimination by the immune system. STA-4783 also acts within the centrosome, a critical component of cellular infrastructure, to disrupt the organization of the cytoskeletal network and the process of cell division. Preclinical studies indicate that STA-4783 acts synergistically with taxane therapy, the most commonly used class of chemotherapeutics.

The preliminary Phase 2 data from the NSCLC trial showed a response rate of 44 percent (7/16), while an additional 38 percent (6/16) of these patients experienced disease stabilization for a total non-progression rate of 81 percent (13/16). Preliminary Phase 2 data from the soft tissue sarcoma trial indicate that 47 percent (14/30) of patients have achieved non-progression of disease at three months. Adverse events reported in both studies have been consistent with those reported from treatment with paclitaxel and carboplatin, or paclitaxel alone.

"We are very encouraged by the data to date from these ongoing, Phase 2 trials in patients with lung cancer and sarcoma - both very difficult to treat diseases," said Matthew L. Sherman, M.D., Senior Vice President and Chief Medical Officer at Synta. "Positive results from both trials in Stage 1 allowed us to advance to Stage 2 of the trials, and we anticipate presenting complete study data for our Phase 2 trials in late 2005 and early 2006."

### **STA-4783 Non-Small Cell Lung Cancer (NSCLC) Trial Design and Results**

The two-stage, Phase 2 trial for the treatment of NSCLC is designed to compare the effect of standard first-line combination lung cancer therapy, paclitaxel and carboplatin, with the effect of this same combination therapy plus STA-4783. Patients included in this study were diagnosed with advanced (stage IIIb or stage IV) NSCLC and had not received prior chemotherapy. In the first stage of this trial, patients received treatment with paclitaxel, carboplatin, and STA-4783 every three

weeks. These three-week cycles were repeated until the earlier of disease progression or completion of six cycles.

Results from the first stage, open-label portion of this trial showed a response rate of 44 percent (7/16). These patients experienced a partial response, defined under the RECIST criteria as a 30 percent or greater reduction in tumor diameter. An additional 38 percent (6/16) of patients experienced disease stabilization, defined as between a 30 percent reduction and a 20 percent increase in tumor diameter, for a total non-progression rate of 81 percent (13/16). Data to date from this trial has also shown that seven of the eight treated patients with evaluable samples showed increased natural killer (NK) cell activity. These increases are in contrast to historical reductions in NK activity following treatment with paclitaxel seen in some clinical trials.

"Non-small cell lung cancer is a very difficult disease to treat, yet we have seen responses in these patients by combining STA-4783 with the leading current first-line therapy," said Dr. Ravi Salgia, coordinating investigator from the University of Chicago. "I am personally encouraged by the responses seen to date and look forward to testing whether additional NSCLC patients could experience clinical benefit from treatment with STA-4783 in combination with paclitaxel and carboplatin."

Stage 1 of this study evaluated two dose levels: 175 mg/m<sup>2</sup> paclitaxel with 233 mg/m<sup>2</sup> STA-4783; and 200 mg/m<sup>2</sup> paclitaxel with 266 mg/m<sup>2</sup> STA-4783. Both dose levels were tolerated and the higher dose level was selected for the randomized Stage 2 portion of the trial. The adverse events seen to date in this trial include anemia, neutropenia, thrombocytopenia, nausea, vomiting, asthenia, fatigue, anorexia, dehydration, myalgia, and alopecia. Similar adverse events are seen in patients treated with paclitaxel and carboplatin alone.

Enrollment and treatment in Stage 2 of the NSCLC trial is complete; 87 patients have been randomized in a blinded fashion to receive the paclitaxel and carboplatin combination with or without STA-4783. Follow-up with these patients is ongoing and complete data from this trial are expected to be available in the second half of 2005.

#### STA-4783 Soft Tissue Sarcoma Trial Design and Results

The two-stage Phase 2 soft tissue sarcoma trial is designed to assess activity based on response and non-progression rates. Because there is no established role for paclitaxel alone in this indication, all patients receive weekly treatments of the combination of paclitaxel and STA-4783 for three weeks, followed by one week of rest. This trial enrolled patients with soft tissue sarcoma who have failed at least one prior chemotherapy treatment.

In the first stage, 47 percent (14/30) of patients have achieved non-progression of disease. The combination was well-tolerated with no drug-related serious adverse events reported. The following related events occurred in more than 10 percent of patients: fatigue, alopecia, nausea, anemia, diarrhea, sensory peripheral neuropathy, peripheral neuropathy, and headache.

Enrollment of 54 additional patients in the second stage of this open-label trial is complete and treatment is ongoing. Additional data are expected to be available in late 2005 or early 2006.

#### STA-4783 Malignant Melanoma Trial

Synta is also currently enrolling patients in a Phase 2 trial of STA-4783 in malignant melanoma. The

two-stage Phase 2 melanoma trial is designed to directly compare treatment of paclitaxel with weekly treatments of paclitaxel plus STA-4783 for three weeks, followed by one week of rest. This trial is enrolling patients with metastatic melanoma who have received up to one prior chemotherapy treatment. Complete data from this trial are expected to be available in late 2005 or early 2006.

### STA-4783 Phase 1 Trial Design and Results

The Phase 1 trial, which enrolled 35 patients, was designed to assess the safety, pharmacokinetics, and efficacy of STA-4783 with paclitaxel in a broad cancer patient population. The combination of STA-4783 and paclitaxel was well-tolerated, with minimal to no toxicity attributed to STA-4783 at all doses tested. The side effects seen were consistent with adverse events typically seen with paclitaxel therapy and included most frequently grade 3 or 4 neutropenia and leukopenia. Partial response or disease stabilization was observed in patients with several cancer types; some of these patients had experienced disease progression after treatment with paclitaxel alone.

Biological markers of activity were also measured in this trial, including levels of circulating Hsp70 in the blood. Time-dependent and dose-dependent increases in levels of Hsp70 following administration of STA-4783 were observed.

### About STA-4783

STA-4783 is a novel, small-molecule compound that Synta is currently evaluating in three separate Phase 2 trials for the treatment of non-small cell lung cancer, malignant melanoma, and soft tissue sarcoma, in combination with taxanes, a leading class of anticancer therapeutic agents. STA-4783 induces the expression of heat shock protein 70 (Hsp70) on the surface of tumor cells, which flags the cells for destruction and elimination by the immune system. STA-4783 also acts within the centrosome, a critical component of cellular infrastructure, to disrupt the organization of the cytoskeletal network and the process of cell division. Preclinical studies indicate that STA-4783 acts synergistically with taxane therapy, the most commonly used class of chemotherapeutics.

### About NSCLC

Lung cancers are diseases characterized by uncontrolled growth where the cancerous cells originate from within the lung. Based on pathology, these tumors are grouped into either small cell or non-small cell lung cancers (NSCLC). Cancer has now become the leading cause of death for Americans under the age of 85, and NSCLC continues to be the leading cause of U.S. cancer-related deaths, accounting for approximately 80 percent of all lung cancers. The American Cancer Society estimated that in 2005, approximately 138,000 people in the U.S. will be diagnosed with NSCLC and approximately 130,000 will die of the disease. Most NSCLC patients are diagnosed with advanced stage disease, where surgery is not a reasonable therapeutic option. The survival rate among advanced NSCLC patients is less than one year.

### About Soft Tissue Sarcoma

Soft tissue sarcoma is a group of cancers in which the malignant cells originate from any of the body's numerous types of soft tissue, such as muscles, connective tissues, blood vessels, lymph vessels, joints, and fat. Surgery can be curative if the disease is diagnosed early, although almost half of patients eventually die of their disease. The American Cancer Society estimated that approximately 9,000 people will be diagnosed with sarcoma and approximately 3,500 will die from

the condition in the U.S. in 2005.

#### About Malignant Melanoma

Melanoma is a serious form of skin cancer that arises from the pigment producing cells of the skin. Although melanoma accounts for only about 5 percent of all skin cancers, it causes most skin cancer related deaths. The American Cancer Society estimated that approximately 60,000 people will be diagnosed with melanoma and approximately 8,000 will die of the disease in the U.S. in 2005. If melanoma is diagnosed early, surgical treatment can often be curative. However, for patients whose disease spreads, the prognosis is poor, with expected survival of approximately seven months.

#### About Synta

Synta Pharmaceuticals Corp. is a biopharmaceutical company focused on discovering, developing, and commercializing small-molecule drugs to extend and enhance the lives of patients with severe medical conditions, including chronic inflammatory disease and cancer. Synta currently has three drug candidates in human clinical trials, as well as a diverse pipeline of internally developed discovery programs. For more information, please see [www.syntapharma.com](http://www.syntapharma.com).