Cytheris Announces 48-Week Results of Phase I/II Study Showing Administration of Interleukin-7 (IL-7) Significantly Improves CD4 T-Cell Counts in Chronically Infected HIV-1 Patients

Additional Results From Two Non-Human Primate Studies Indicate IL-7 Administration May Provide Therapeutic Route To Stable Disease

Paris – February 13, 2008 – Cytheris SA, a clinical stage biopharmaceutical company focused on research and development of new therapies for immune modulation, today announced results of the long-term follow-up of patients in a multi-center Phase I/II study designed to investigate the safety of Interleukin-7 (IL-7) therapy in chronically HIV-1 infected patients whose $CD4^+$ T-cell counts remained low despite treatment with anti-retroviral-therapies (HAART). After 48 weeks, patients treated at the higher dose level showed a median increase in $CD4^+$ and $CD8^+$ T-cell counts (cells/µL) of 75% and 57%, respectively, from baseline levels. Additionally, two posters detailing non-human primate studies of IL-7 immunotherapy and early T-cell homing to the gut were presented at the 2008 Conference on Retroviruses and Opportunistic Infections (CROI) held last week in Boston.

The results of the Phase I/II long-term follow-up study (Abstract #708) were presented by Pr. Yves Lévy MD, PhD (Hôpital Henri Mondor, Créteil, France and INSERM), Principal Investigator. This long-term follow-up investigation indicates the stability of the T-cell response already noted at week 12 of the study and previously reported by Dr. Lévy at CROI in 2007.

"In the long-term follow-up of this study, IL-7 administration significantly improves CD4 T-cell counts in patients who entered the study with low CD4 counts, opening them to potentially fatal opportunistic infections," said Dr. Michel Morre, President and CEO of Cytheris. "If we can restore normal levels of CD4 in these HIV-infected patients undergoing HAART therapy, IL-7 may then become an important therapeutic option in the treatment of HIV as a chronic disease, allowing these patients to potentially achieve a normal lifespan. These results thus reinforce interest in continuing clinical investigation of IL-7 for treatment of HIV infection."

48-Week Results of Phase I/II Study

The hallmark of HIV infection is a defect in the function and homeostasis of $CD4^+$ T lymphocytes leading to the development of opportunistic infections and malignancies. IL-7 plays multiple roles in the differentiation, expansion and survival of T-cells. Studies in animal experimental models have shown that IL-7 can enhance the proliferation and expansion of T lymphocytes. By its action, IL-7 may provide a novel approach for the restoration and/or improvement of the $CD4^+$ T-cell pool and immune functions in patients infected with HIV.

The Phase I/II trial was designed to investigate the safety of IL-7 therapy in chronically HIV-1 infected patients with low CD4 counts (100-400 $CD4^+$/µl) and plasma HIV RNA <50 cp/ml for at least 6 months while on HAART. Six and 7 patients were included in the first (3 µg/kg) and second (10 µg/kg) dose level, respectively. Patients received 8 subcutaneous injections (3 times/week; days 1-16) of r-hIL-7. Clinical, biological and virological safety parameters were monitored until week 48. HIV Gag-specific T-cell responses were assessed by intra-cellular cytokine staining in the 10 µg/kg group.

The long-term results for this group of patients, defined as "immune non-responders", indicate that the IL-7 induced rapid expansion of $CD4^+$ and $CD8^+$ T-cell counts was sustained up to 48 weeks from study entry. Importantly, 48 weeks after initiation of this IL-7 short course of treatment, patients treated at the 10 µg/kg dose level showed a median increase in $CD4^+$ and $CD8^+$ T-cell counts (cells/µL) of 75% and 57%, respectively, from baseline levels.

Results of Non-Human Primate Studies

The IL-7 induced T-cell proliferation indicated in the long-term follow-up to the Phase I/II study discussed above is now broadly confirmed by numerous studies in non-human primates such as the two poster presentations discussed here. These studies were conducted in collaboration with the Seattle Biomedical Research Institute (SBRI), the Vaccine and Gene Therapy Institute (VGTI) and the Oregon National Primate Research Center (ONPRC) at Oregon Health and Science University, Emory University (Abstract #707) and the Institut Pasteur, Paris (Abstract #709).

These two studies were designed to analyze the potential of IL-7 treatment to facilitate reconstitution in the deep lymphoid tissues such as lymph nodes and G.I. tract. In both human HIV and simian SIV infection it has been shown that $CD4^+$ T-cell depletion occurs quickly and primarily in the gut. Of particular note is that in these simian models, "elite controllers" (ECs), rare individuals who spontaneously control HIV viremia to levels below the detection threshold of current assays, consistently show good T-cell repopulation of the gut. In these two studies, not only did IL-7 confirm its potential for T-cell expansion, but it also showed its ability to send T-cells to the gut mucosa where it also triggers local T-cell expansion. Numerous experimental and clinical studies have shown that T-cell reconstitution in the gut is critical for restoring control over the HIV virus.

Summary of Presentation Results

These findings based on animal models and human studies emphasize the potential stability of the IL-7 effect on the production of T-cells over time as well as its possible impact in stimulating T-cell proliferation in the lymphoid tissue layer in the mucous membrane of the GI tract.

Taken together, these studies suggest that administration of IL-7 may have an important effect on immunologic recovery in HIV-infected patients whose HAART regimens have been unsuccessful in restoring $CD4^+$ T-cells to a stable level. These "Immune Non Responders," patients with progressive or unstable disease, are in marked contrast to nonprogressors or "elite controllers" who, like their simian counterparts noted above, show no evidence of HIV progression and have stable $CD4^+$ T-cell counts even after years of HIV infection. The sustained immunological efficacy seen in the long-term follow-up of the Phase I/II study suggests that a short course of IL-7 treatment may provide an important avenue for enhancing the immune system and inducing broad spectrum proliferative activity of $CD4^+$ and $CD8^+$ T-cells in the blood, lymph nodes and small intestine, a key therapeutic effect in achieving long term disease stability in HIV-infected patients.

About Cytheris – www.cytheris.com
Cytheris SA is a privately held clinical-stage biopharmaceutical company focused on research and development of new therapies for immune modulation. These drugs aim at reconstituting and enhancing the immune system of patients suffering from cancer, chronic viral or bacterial infections such as HIV and HCV, or lympho-depleting treatments such as chemotherapy, radiotherapy, bone marrow transplantation (BMT) and hematopoietic cell transplantation (HCT).

The company's lead compound, recombinant human Interleukin-7 (r-hIL-7), is a critical growth factor for immune T-cell recovery and enhancement. Clinical trials conducted on more than 60 patients in France and the U.S. have already demonstrated the ability of r-hIL-7 to expand and protect $CD4^+$ and $CD8^+$ T-cells. The Company is currently conducting multiple clinical studies of IL-7 in HIV, HCV and cancer.

A second family of products being developed by the company is based on highly potent NKT/dendritic cell ligands in-licensed from New York University, the Aaron Diamond AIDS Research Center and the City University of New York. NKT cells have been implicated in many diverse aspects of immunity, including regulation of autoimmune disorders, control of tumor growth and spread, and defense against a number of pathogens. The product family strengthens innate and adaptive immunity connections and will provide new immuno-therapeutic adjuvants for cancer and chronic infectious diseases.

The company operates from its headquarters and laboratories in Issy-les-Moulineaux, a suburb of Paris, and its U.S. subsidiary in Rockville, Maryland.

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