



Cytheris Initiates INSPIRE 2, a Phase II Clinical Trial of Recombinant Human Interleukin-7 (CYT107) in Chronically Infected HIV Patients Who Fail to Achieve Optimal Immune Reconstitution under HAART Therapy

Study is designed to confirm the safety profile, pharmacokinetics and immunological effects previously shown in the first INSPIRE study and to explore the impact of CYT107 on HIV specific T cell responses

Paris (France) – 12 January, 2010 – Cytheris SA, a clinical stage biopharmaceutical company focused on research and development of new therapies for immune modulation, today announced that it has begun enrolling patients in INSPIRE 2, a Phase IIa clinical program evaluating the company's investigative immune-modulator, recombinant human Interleukin-7 (CYT107), in the treatment of chronically HIV-1 infected patients classified as Immunological Non Responders (INR) after at least 12 months of highly active anti-retroviral therapy (HAART). The phase IIa study is designed to evaluate the biological activity and pharmacokinetic (PK) profile of CYT107 at a dose of 20 µg/kg/week in patients with CD4 counts of 101-400 cells/µL. The study will be conducted across 4 investigative sites in the United States and Canada.

"In most HIV patients, the first year of HAART therapy effectively suppresses viral replication but does not result in restoration and maintenance of CD4 T-cell counts above 500 cells/mm³, the threshold accepted as indicative of sufficient immune reconstitution in this patient population," said Michel Morre, DVM, President and CEO of Cytheris. "In fact, some 30% of these patients will never achieve the 500 cells/mm³ level even after years of HAART treatment."

As demonstrated in large patient cohorts, the risk of disease progression or death in patients who remain below the 500 cells/mm³ level is significantly higher when compared to patients who achieve an optimal T-cell restoration with CD4 > 500 cells/mm³. INSPIRE 2 is being launched to confirm the unique ability of CYT107 to trigger and support immune reconstitution in these patients as already documented in the first INSPIRE study.

"We anticipate that we will see substantial increases in circulating CD4 T cell counts in patients whose CD4 T-cell counts were not restored to normal levels despite complete control of HIV replication under HAART," said Michael M. Lederman, MD, the Scott R. Inkle Professor of Medicine at Case Western Reserve University, Cleveland, Ohio, Associate Director, CWRU/UHC Center for AIDS Research, and Principal Investigator-Coordinator/Study Chairman for the trial.

"This phase IIa confirmatory study is designed to further demonstrate the biological activity of CYT107 and provide data that will help in the design of phase IIb/III trials," said Thérèse Crougns, MD, Chief Medical Officer of Cytheris, "The study objectives include characterization of CYT107 pharmacokinetics and pharmacodynamics in patients with moderate to severe lymphopenia, delineation of the relationship between CYT107 dose and biological activity, and confirmation of the relevance of the treatment schedule evaluated in the first INSPIRE study reported on at the recent ICAAC meeting."

Data from the first INSPIRE study were presented by Yves Levy, MD, PHD [Scientific Director of the French National Agency for Research on AIDS and Viral Hepatitis (ANRS) Vaccine Program, Service d'Immunologie Clinique, Hôpital Henri Mondor, Créteil, France and Inserm, Principle Investigator and Co-Chair of the INSPIRE study] during an oral late breaker session at the 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held September 12-15, 2009, in San Francisco, CA (Abstract H-1230a). The analysis shows that CYT107 induces a dose dependent and sustained increase of CD4 T-cells, with many patients achieving CD4 counts > 500 cells/mm³. The median CD4 and CD8 T-cell increases per mm³ over baseline, from 240 to 563 (135%) and from 659 to 1210 (65%), respectively, at the 20mcg/kg dose, suggest the potential of CYT107 to play a significant role in HIV therapy and represent part of the rationale for initiating the INSPIRE 2 study to further explore the immunological properties of CYT107.

About the Study (CLI-107-13)

INSPIRE 2 is an open-label, multicenter study of subcutaneous intermittent recombinant Interleukin-7 (CYT107) in chronically HIV-infected patients with CD4 T-lymphocyte counts between 101-400 cells/mm³ and plasma HIV RNA < 50 copies/mL after at least 12 months of HAART.

The primary objective of the study is to determine in detail the biological activity and PK profile of CYT107 (20 µg/kg/week), during a 12-week study period with a follow up period of up to 1 year, in an HIV-infected cohort with CD4 counts of 101-400 cells/µL. The dose of 20 µg/Kg/week that will be evaluated in this study has shown a good safety profile and biological activity in the first INSPIRE study (CLI-107-06) conducted in a similar population.

Secondary objectives are:

- To characterize the pharmacokinetics and pharmacodynamics of CYT107 in the targeted population.
- To further evaluate the safety profile established with CYT107 at 20µg/kg. Safety assessments will include a close monitoring of the impact OF CYT107 on HIV RNA viral load and immunogenicity.
- To further evaluate the immunological effects established with CYT107 at 20µg/kg.

- To document the potential sustained CD4 increase achieved at D21, D28, Weeks 9 and 12 (“targeted sustained activity”).
- To document safety and sustained CD4 increase quarterly until the end of the first year.
- To document other immunological properties of IL-7, (i.e. T-cell homing within the lower GI tract).

About Interleukin-7 (CYT107)

Recombinant human interleukin-7 (CYT107) is a critical immune-modulator for immune T-cell recovery and enhancement. As a growth factor and cytokine physiologically produced by marrow or thymic stromal cells and other epithelia, IL-7 has a critical and, at some steps, a non-redundant stimulating effect on T lymphocyte development, notably on thymopoiesis and, downstream from the thymus, on homeostatic expansion of peripheral T-cells.

A first-generation form of rhIL-7 was shown in pre-clinical and Phase I studies in oncology and HIV-infected patients to be well tolerated in repeated dose trials, with long-lasting increases in both CD4 and CD8 T cells. CYT107 is a second-generation rhIL-7 product made by Cytheris via a recombinant mammalian cell culture system.

Clinical trials conducted on more than 120 patients in Europe, North America and Taiwan have demonstrated the potential of IL-7 to expand and protect CD4+ and CD8+ T-cells.

Currently, Cytheris is conducting multiple international investigations of IL-7 in HIV, HBV, HCV, idiopathic CD4 lymphocytopenia (sponsored by NIAID/NIH) and cancer, the latter including an NCI/NIH-sponsored study of IL-7 in combination with dendritic cell vaccines in a pilot study of tumor vaccination in children, and a study designed to restore CD4+ and CD8+ counts following T-cell depletion due to bone marrow or peripheral blood stem cell transplant (being conducted at the Memorial Sloan-Kettering Cancer Center in New York City).

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 HCV, HBV and HIV, or lympho-depleting treatments such as chemotherapy, radiotherapy, bone marrow transplantation (BMT) and hematopoietic cell transplantation (HCT). 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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