



## **Cytheris Expands Interleukin-7 Clinical Development Program With International Phase I/IIa Trial In HIV**

### **Company Provides Update at Stockholm Symposium Sponsored by Nobel Forum Following Earlier Initiation of Trials in Hepatitis C and Oncology**

Paris, September 26, 2007—Cytheris, a clinical stage biopharmaceutical company focused on research and development of new therapies for immune modulation, today announced expansion of the clinical trial program for CYT107, the company's recombinant human Interleukin-7 (IL-7), with the initiation of a Phase I/IIa clinical trial in HIV patients. The trial will be conducted at sites in France, Italy, Canada and the United States and follows the launch of previously announced Phase I/IIa trials of IL-7 in Hepatitis C (HCV) and oncology. These trials also follow the successful completion of four Phase I studies and are designed to investigate IL-7's potential for building immune system response.

The announcement was made at the mini-symposium entitled "[Interleukin-7 in Health and Disease](#)" in the series 'Frontiers in Medicine' at the Nobel Forum, Karolinska Institutet, held in Stockholm, Sweden, September 17–18, 2007.

The Forum brought together twelve invited speakers before an international audience to review and exchange results on IL-7 biology, cell functions, receptors and key preclinical and clinical results. Cytheris President and CEO, Michel Morre, DVM, announced the start of the Phase I/IIa trial in HIV and presented promising preclinical and clinical results obtained in cancer and HIV. Morre's presentation was part of the section devoted to IL-7 clinical development chaired by Markus Maeurer, Professor of Clinical Immunology at the Karolinska Institutet,

Forum participants expressed particular interest in pursuing various avenues of IL-7 investigation including: 1) Oncology, in association with chemo- and immunotherapy; 2) HIV infection, to reconstitute the immune system and trigger an anti-viral response, potentially limiting the incidence of AIDS-related and non-related pathologies; 3) HCV infection, to speed viral clearance and increase the proportion of patients able to clear the virus; and, 4) various other chronic infections such as tuberculosis.

"We are happy to see the Nobel Foundation hold the first international meeting exclusively dedicated to IL-7," said Morre. "The exchanges between top international experts confirm the therapeutic potential of this cytokine in the treatment of immune compromised patients suffering from lymphopenia as well as cancer and chronic viral infections. Progressively, a large set of results derived from cell biology, preclinical and now clinical studies demonstrates the therapeutic potential of IL-7. Our new Phase I/IIa studies in HIV, oncology and HCV are designed to further document these effects."

### **About the HIV Study**

The HIV trial (CYT107-06) is a randomized placebo controlled, single-blind multi-center dose-escalation study of chronically HIV-infected patients with CD4 T-lymphocyte counts between 101-400 cells/mm<sup>3</sup> and plasma HIV RNA < 50 copies/mL after at least 12 months of Highly Active Anti-Retroviral Therapy (HAART). The trial will be conducted at sites in the US, Canada, France and Italy.

Michael M. Lederman, MD, the Scott R. Inkley Professor of Medicine and Director of the Case Western Reserve University/University Hospitals Center for AIDS Research, Cleveland, Ohio, will chair the study along with co-chairs Irini Sereti, MD, US National Institute for Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, and Yves Levy, MD, PhD, Service d'Immunologie Clinique, Hôpital Henri Mondor, Créteil, France.

Results of two promising Phase I studies of Cytheris' IL-7 in HIV patients, one conducted by Dr. Levy's team and the other by the US National Institutes of Health/AIDS Clinical Trials Group (ACTG), were reported at the 2007 Conference on Retroviruses and Opportunistic Infections (CROI) held in Los Angeles.

### **About the Oncology Study**

The oncology trial (CYT107-04) targets patients with metastatic melanoma or advanced renal cell carcinoma. This dose escalation study, to include 18 to 30 patients both lymphopenic and non-lymphopenic, is being conducted at the US National Cancer Institute (NCI) in Bethesda, Maryland, in collaboration with Steven A. Rosenberg, MD, PhD, (principal investigator).

Dr. Rosenberg is Chief of Surgery at NCI and a Professor of Surgery at the Uniformed Services University of Health Sciences and at the George Washington University School of Medicine and Health Sciences in Washington, D.C. He is recognized as a pioneer in the development of immunotherapy that has resulted in the first effective immunotherapies for selected patients with advanced cancer. Most recent clinical data demonstrate how critical the immunological status of cancer patients is for their clinical outcome. CYT107 is expected to boost patient immune responses against their tumor. This will be important in the treatment of post-chemotherapy residual diseases and/or to support efficacy of various cancer vaccine approaches.

Dr. Rosenberg has previously reported (*J Immunother* (1997) 2006; 29(3): 313-319) the promising results of a Phase I clinical trial of Cytheris' IL-7 in cancer patients, concluding that the study "demonstrates that IL-7 is a potent lymphopoietic factor in humans and has substantial potential for use in the treatment of patients developing lymphopenia from HIV infection or from chemotherapy used in cancer treatment. The selective increase in non-T-regulatory CD4<sup>+</sup> T cells represents a significant advantage of the use of this cytokine".

### **About the HCV Study**

The HCV trial (CYT107-05) focuses on patients who are non-responders to the reference treatment (12 weeks of PEG-interferon + ribavirin). This multi-center dose escalation study conducted at sites in Switzerland, France and Italy will include 12-18 patients who will receive weekly injections of CYT107 over a four-week period in addition to the reference treatment. More than one-third of patients do not respond to the reference treatment because they are unable to mount an efficient immune response against the virus. Cytheris expects the addition of CYT107 treatment will restore appropriate T cell function and help these patients better cope with the virus.

Tilman Gerlach, MD, Clinic for Gastroenterology and Hepatology, Zurich University Hospital, Zurich, Switzerland, will chair the study; Patrick Marcellin, MD, Head of the Claude Bernard Research Center on Viral Hepatitis, Service d'Hépatologie and INSERM Unit 481, Hospital Beaujon, Clichy, is the French Coordinating Investigator; Giuseppe Tambussi, MD, Division of Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy, will be the Principal Investigator for the Italian study site; and Roberto Speck, MD, Division of Infectious Diseases and Hospital Epidemiology, Zurich University Hospital, will be responsible for conducting the immunological research.

### **About CYT107, Recombinant Interleukin-7**

Interleukin-7 (IL-7) is a multifunctional cytokine, mainly produced by non-hematopoietic cells, which is active notably but not only on T cell development. IL-7 has a critical and, at some points, a non-redundant stimulating effect on T lymphocyte development, on thymopoiesis and downstream from the thymus, on homeostasis expansion of peripheral T cells.

At least two properties of IL-7 justify its development as a drug, both in oncology and infectious disease:

- A quantitative effect consisting of a massive expansion of T cells, which not only contributes to improved immune recovery but also to the elimination of tolerance for chronic stimulation by virus- or tumor-derived antigens;
- A functional enhancement of  $\alpha\beta$ -T cell reactivity to weak immunogens, such as proteins or virus causing chronic infections or tumor-associated antigens.

This broad activity of IL-7 leads to the consideration of several avenues of development for CYT107:

- The restoration of the immune system and the prevention of opportunistic infections in patients who develop severe lymphopenia, such as in HIV infection or treatment with lympho-ablative chemo- or radio-therapies;
- The control of chronic viral infections such as HIV and HCV or in the treatment of cancers, either in the minimal residual disease or in more advanced tumors, where IL-7 could be used as a stand-alone agent or in combination with other immunotherapeutic agents, notably with vaccines or as an adjunct to antiviral drugs.

## **About Cytheris**

Cytheris SA is a 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 (e.g. post-chemo, -BMT and -HCT).

The company's lead compound, recombinant Interleukin-7 (rIL-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 US have already demonstrated the impressive ability of rIL-7 to expand and protect CD4+ and CD8+ T cells.

A second family of products is based on highly potent NKT/dendritic cell ligands in-licensed from several New York universities. The product family strengthens innate and adaptive immunity connections and will provide new immunotherapeutic adjuvants for cancer and chronic infectious diseases.

The company operates from its headquarters in Issy-les-Moulineaux, a suburb of Paris, and its US subsidiary in Rockville, Maryland. For additional information about the company, please visit: [www.cytheris.com](http://www.cytheris.com).

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