Cytheris Announces Interim Data From INSPIRE Study Showing Interleukin-7 (CYT107) Induces Dose-Dependent and Sustained Increase of CD4 T Cells in Chronic HIV-Infected Patients

Phase I/IIa data at week 12 show more patients experienced CD4 counts > 500 cells/mm^3 when treated at 20mcg/kg dose

Paris (France) – September 15, 2009 – Cytheris SA, a clinical stage biopharmaceutical company focused on research and development of new therapies for immune modulation, today announced presentation of data from an interim analysis of CLI-107-06 (INSPIRE), a Phase I/IIa study of HIV-infected patients with low CD4 T cell counts. The patients were treated with a three-injection cycle of the Company's investigative immune-modulator, recombinant human Interleukin-7 (CYT107). The analysis shows that CYT107 induces a dose dependent and sustained increase of CD4 T cells with many patients achieving CD4 counts > 500 cells/mm^3. The INSPIRE data were presented 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).

"Even in the HAART era, it appears that low CD4 T cell counts place HIV infected persons at greater risk for a variety of serious morbidities. This study shows that treatment with IL-7 can increase CD4 T cell counts in many of these patients to levels that are within the "normal" range. We now need to know whether these increased CD4 T cell counts confer protection from these serious complications," said Michael M. Lederman, MD, the Scott R. Inkley Professor of Medicine at Case Western Reserve University, Cleveland, Ohio, Associate Director, CWRU/UHC Center for AIDS Research, and Chairman of the INSPIRE study.

"The interim results with CYT107 closely mimic and even improve upon those seen in a recently published study[1] in chronic HIV-infected patients treated with an earlier, non-glycosylated version (CYT 99 007) of Cytheris' IL-7," said 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, Presenter, Principle Investigator and Co-Chair of the INSPIRE study. "These results show that 3 injections of IL-7 are sufficient to expand naive and memory T cells in the long term. Further studies are needed to demonstrate whether these biological effects translate into clinical benefits."

About the Study (CLI-107-06)
INSPIRE is a Phase I/IIa randomized placebo controlled, single-blind multicenter (Europe, US, and Canada) dose-escalation study of subcutaneous intermittent glycosylated Interleukin-7 (CYT107) in chronically HIV-infected patients with CD4 T-lymphocyte counts between 101-400 cells/mm^3 and plasma HIV RNA< 50 copies/mL after at least 12 months of HAART. Patients selected in this trial are categorized as immunological low or non responders (INR), i.e. patients who have not optimally restored their immunity despite at least 12 months of HAART and with complete control of HIV replication.

INR patients represent from 5 to 30% of the HIV treated population, the prevalence of which depends on the definition criteria, which are used to characterize them. As shown in large cohorts, the risk of disease progression or death is significantly higher in the INR sub-population when compared to patients who achieve better T cell restoration.

Methods: Chronically HIV-infected patients with 101-400 CD4 cells/mm^3 and plasma HIV RNA< 50 cp/mL while on ART received three weekly subcutaneous injections of CYT107. Three doses were tested: 10, 20 or 30 µg/kg/week (8 patients CYT107 vs 2 placebo per dose). Phenotypic analyses of T cell subsets and thymopoiesis surrogate markers (RTE and sj/βTRECs ratio quantification) were performed.

Results: No clinical or laboratory side effects > grade 2 were recorded. In the 20µg/kg group, 4 patients experienced a transient increase of HIV RNA values (<500 cp/mL in 3 of 4 and 1023 cp/mL in 1). The biological activity of CYT107 is shown below:

10µg/Kg	**Baseline** (median T cells/mm^3)	**Day 28** (median T cells/mm^3; % increase)	**Week 12** (median T cells/mm^3; % increase)	**P value Baseline vs W12** (Wilcoxon test)
CD4	268	643 (152%)	419 (87%)	**0.006**
CD8	761	1434 (91%)	1081 (42%)	**0.006**
Naive CD4	41	82	93	**0.016**
RTE CD4	3	6	4	NS
Sj/βTREC ratio	12	18	25	NS
20µg/Kg				
CD4	240	709(205%)	563 (135%)	**0.004**
CD8	659	1695 (131%)	1210 (65%)	**0.004**
Naive CD4	66	218	136	**0.016**
RTE CD4	5	21	5	NS
Sj/βTREC ratio	17	36	26	**0.062**

(Total and naïves CD4 and CD8 increases are statistically significant vs. placebo group (P<0.005). 1/7 and 5/8 of pts experienced CD4 counts > 500 cells/mm^3 at week 12 (P<0.005) at the 10 and 20mcg/kg dose respectively.)

Conclusions: A three-injection cycle of CYT107 induces a dose dependent and sustained increase of CD4 T cells. A higher proportion of patients experienced CD4 T cell counts > 500 cells/mm^3 and a trend toward higher thymic output at the 20mcg/kg dose.

The design of the trial allows for an assessment of potential individual benefits in patients whose CD4 T cell count is suboptimal at baseline despite complete control of HIV replication under HAART. Such benefit may correspond to a sustained expansion of CD4 T cells, and potentially, a decrease in morbidity and mortality which is increased in this sub-population of patients compared to those who restore a higher CD4 T cell count after several months of HAART.

"The interim analysis of INSPIRE data presented here further strengthens the potential role of CYT107 as a potent and safe immune modulator which is capable of dramatically increasing both CD4 and CD8 T cell counts in HIV-infected patients," said Thérèse Croughs, MD, Chief Medical Officer of Cytheris. "The median CD4 and CD8 T cell increases per mm^3 over baseline, from 240 to 563 (135%) and from 659 to 1210 (65%), respectively, at the 20mcg/kg dose, clearly indicate the potential of this cytokine to play a significant role in HIV therapy and more than justifies its further clinical development."

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 non-glycosylated form of rhIL-7 (CYT 99 007) 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 glycosylated rhIL-7 product made by Cytheris via a recombinant mammalian cell culture system.

Clinical trials conducted on more than 110 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 HCV, HIV and cancer, with trials for other indications planned to initiate in 2H09.

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.

(1) Lévy, Y et al, "Enhanced T cell recovery in HIV-1-infected adults through IL-7 treatment" *The Journal of Clinical Investigation*, 2009, Vol. 119, No. 4: 997-1007.

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