



Cytheris Announces Publication of IL-7 Oncology Data in *The Journal of Experimental Medicine*

Results of a second phase 1 trial in oncology further demonstrate the potential of Interleukin-7 to induce dramatic and prolonged CD4 and CD8 T cell expansion

Paris – June 26, 2008 – Cytheris SA, a clinical stage biopharmaceutical company focused on research and development of new therapies for immune modulation, today announced the publication of data from a phase 1 dose escalation study evaluating the effects of IL-7 therapy on human lymphocytes in subjects with non-hematologic, non-lymphoid cancer refractory to standard therapy. The results of this study, performed in collaboration with U.S. National Cancer Institute (NCI) investigators lead by Claude Sportès, Crystal Mackall and Ronald Gress, support the potential of the IL-7 investigational product as an immunotherapy for the treatment of patients with impaired immunity due to physiologic (age), iatrogenic (chemotherapy or transplantation) or pathologic (HIV) lymphodepletion.

“Impaired immune reconstitution remains a significant medical problem in many clinical settings due to the fact that no agent able to safely expand a broad repertoire of T cells has yet been identified,” said Michel Morre, DVM, President and CEO of Cytheris. “This study demonstrates that IL-7 administration can safely induce polyclonal T cell expansion resulting in dramatic increases in T cell number, supporting the potential of IL-7 as a clinically effective T cell growth factor. We are especially pleased with these results as they reflect our long term and productive collaboration with NCI.”

The paper entitled “Administration of rhIL-7 in Humans Increases in vivo TCR Repertoire Diversity by Preferential Expansion of Naïve T cell Subsets” is published in the June issue of *The Journal of Experimental Medicine* (Sportès, C et al, 2008, Vol. 205, No. 6:10.1084/jem.20071681). The full article can also be found online at the JEM website at <http://www.jem.org>.

Summary results are as follows:

- This study demonstrates that recombinant human Interleukin-7 (rhIL-7) therapy in humans induces dramatic, polyclonal, prolonged CD4+ and CD8+ T cell expansion *in vivo* with preferential increases in T cells bearing diverse TCR repertoire specificities.
- The effects are mediated primarily through increased peripheral T cell cycling and augmented cell survival.
- The rhIL-7 expanded T cells retain significant functional capacity and the CD4+ T cell expansion is not accompanied by a disproportional increase in Tregs as occurs following rhIL-2 therapy.
- RhIL-7 appears to be an effective T cell growth factor with “immune rejuvenating” properties that suggest it would be effective in augmenting immune reactivity in hosts with impaired immunity due to physiologic (age), iatrogenic (chemotherapy/transplantation) or pathologic (HIV) lymphodepletion.
- In immunologically normal as well as deficient hosts, rhIL-7’s capacity to augment responses to weak antigens and to increase T cell cycling without Treg expansion may be clinically exploitable in the context of immunotherapy regimens for cancer and/or chronic infection.
- The authors further note that lymphopenia induced by cytotoxic chemotherapy or other insults can significantly diminish immune function. In adults, CD4+ T cell recovery following severe immune depletion requires the re-emergence of a pool of naïve T cells which requires 18 to 24 months and may occur only in individuals younger than 40 to 45 years.
- Thus, a therapeutic approach to accelerate, or simply promote in older individuals, the recovery of a widely diverse T cell repertoire may find a multitude of clinical applications.
- If rhIL-7 therapy in humans can augment immune responses to weak antigens, hasten reconstitution of naïve T cell populations and spare Treg expansion, in particular but not restricted to older individuals, it could improve the effectiveness of immune based therapies for cancer or chronic infection in various populations with iatrogenic (chemotherapy), pathologic (HIV) or physiologic (aging) immune insufficiency.

About Interleukin-7

Investigational recombinant human Interleukin-7 (r-hIL-7) is a critical growth factor for immune T-cell recovery and enhancement. Cytokines that signal via the common gamma chain (γ_c) represent promising therapeutics based upon their potential to augment T cell expansion and increase the effectiveness of immune based therapies. Within this family, IL-7 is a prototypic homeostatic cytokine, produced constitutively by nonlymphoid cells. Its receptor (IL-7R α) is expressed on resting T cells, then rapidly down-regulated following T cell activation or IL-7 signaling.

IL-7 is essential for T cell development in mice and humans and for T cell homeostasis since it is required to maintain naïve CD4+ and CD8+ T cells *in vivo*. IL-7 levels rise in serum and tissues following T cell depletion and fall upon recovery.

In preclinical studies, IL-7 therapy exerts marked effects on T cell immune reconstitution in mice and primates. IL-7 augments effector and memory responses to vaccination in mice with preferential enhancement of responses to weak subdominant antigens. In preclinical models, IL-7 therapy augments anti-tumor responses leading to improved survival when combined with anti-tumor vaccines.

Clinical trials conducted on more than 75 patients in Europe and North America have suggested the potential of r-hIL-7 to expand and protect CD4+ and CD8+ T-cells. Cytheris is currently conducting multiple clinical studies of IL-7 in HIV, HCV and cancer.

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 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.

For more information, please contact:

French/International media inquiries -- Andrew Lloyd & Associates:

Andrew Lloyd (allo@ala.com), Juliette dos Santos (juliette@ala.com)

Tel: +33 1 5654 0700

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