Cytheris Announces Publication of Clinical Case Study Combining Recombinant Human Interleukin-7 (CYT107) with Antiviral Agent CMX001 as Potential Treatment for Progressive Multifocal Leukoencephalopathy (PML)

Combination therapy with two investigational agents, Cytheris' CYT107 and Chimerix's CMX001, indicates potential for clearing the JC virus that causes PML, a rare and usually fatal neurological disease

Paris – November 30, 2010 – Cytheris SA, a clinical-stage biopharmaceutical company focused on research and development of new therapies for immune modulation, today announced the publication of a case study report based on successful treatment of Progressive Multifocal Leukoencephalopathy (PML) with combination therapy consisting of two investigational agents, Cytheris' recombinant human interleukin-7 (CYT107) and CMX001, an investigational, oral broad-spectrum antiviral drug (Chimerix, Research Triangle Park, NC) in the *Journal of Antimicrobial Chemotherapy*. The combination therapy succeeded in eradicating the polyomavirus JC, the virus that causes PML, in less than two weeks following initiation of CYT107 treatment, and four weeks following the introduction of CMX001.

Progressive Multifocal Leukoencephalopathy (PML) is a rare and usually fatal neurological disease caused by the polyomavirus JC. The virus, first identified in 1971, multiplies in and destroys oligodendrocytes, which are cells of the brain that produce the myelin sheath surrounding neurons. Symptoms include loss of vision, impaired speech, paralysis, cognitive decline and weakness. There is no known cure for PML.

"The combination of CYT107 with a powerful antiviral agent to treat PML follows the same therapeutic regimen that Cytheris is investigating in clinical studies of HCV and HBV, where interferon or antiviral therapy is employed to drop the viral load and is then followed by added treatment with CYT107 to clear the virus, a process accompanied by an increase in CD4 and CD8 T cell counts", said Michel Morre, DVM, President and Chief Executive Officer of Cytheris. "In responding patients, comparison of the resulting trend lines in decreased viral load and increased CD4 count over time shows an almost identical pattern when the PML case described in Dr. Patel's report is compared to CYT107-treated patients who have cleared the HCV virus. We believe the same pattern will soon emerge as we reach the higher dose range in our HBV CONVERT study, currently being conducted in France and Italy."

The paper, "A case of progressive multifocal leukoencephalopathy and idiopathic CD4+ lymphocytopenia," published in the *Journal of Antimicrobial Chemotherapy* (Patel A, et al, 2010, Dec., Vol. 65(12): 2489-92), is a case study that provides an overview of the treatment of a single adult patient with PML, a rare and usually fatal disease caused by the human polyomavirus JC. The patient, an adult female admitted to The Methodist Hospital, Houston, Texas, was treated by a medical team under the direction of Julie Y. Patel, MD, of the Immunology, Allergy & Rheumatology Department of Texas A&M Health Science Center College of Medicine.

"Though both experiential and experimental data in the treatment of PML have grown quite considerably in recent years, it is important to keep in mind that there still are no known interventions that can reliably prevent or adequately treat PML", stated Dr. Patel. "To my knowledge, this is the first case report to demonstrate the use of combination therapy, in this instance two investigational medications, as a possible therapeutic strategy for the treatment of PML."

About the Case Study
The patient in the reported case study is a 69 year-old female who first presented with mouth numbness. Over the next few months her symptoms progressed to right arm and leg weakness and she eventually developed slurred speech. A brain biopsy showed PML and her cerebrospinal fluid PCR was positive for the JC virus. In addition, her absolute CD4 count was 87 and she was subsequently diagnosed with idiopathic CD4 lymphocytopenia (ICL), a rare disease characterized by abnormally low CD4 T cell counts without evidence of human immunodeficiency virus (HIV) infection.

Prior to IL-7 therapy, she was started on CMX001. Given the risk of deterioration of her condition in the setting of immunodeficiency, Dr. Patel applied for and received an additional Emergency Investigational New Drug Application (EIND) from the U.S. Food and Drug Administration for administration of CYT107 in combination with CMX001, an orally-administered, broad-spectrum antiviral agent with demonstrated in vitro activity against multiple double-stranded DNA (dsDNA) viruses, including cytomegalovirus, adenovirus, JC virus and variola.

Under development by Chimerix, Inc. (http://www.chimerix.com), CMX001 is in Phase 2 clinical studies in immunocompromised transplant and cancer patients for the treatment of life-threatening viruses, including cytomegalovirus and adenovirus. It has also been administered to more than 120 patients under investigator-held Emergency Investigational New Drug applications (EINDs) for the treatment of a wide range of life-threatening infections caused by dsDNA viruses for which there are either no approved treatments or where patients have failed the available treatment.

A treatment cycle of CYT107 includes three administrations of the drug, one subcutaneous injection per week for three weeks. The standard dose is 20µg/kg but to be cautious 10µg/kg was prescribed in this first patient with PML. Shortly after the first administration of CYT107 on March 15, the viral load of this patient dropped to an undetectable level. The patient received the remaining two injections on March 22 and March 29. In September 2010, following submission of the case study for publication, the patient received another cycle of CYT107 to further boost her CD4 T cell count. Blood samples taken during this second cycle of CYT107 administration indicate that the patient remains free of any detectable trace of the JC virus and that her CD4 T cell count continues to increase.

About PML
PML is a rare, progressive, demyelinating disease of the central nervous system that leads to death or severe disability. PML is caused by activation of the John Cunningham (JC) virus. The JC virus resides in latent form in up to 90 percent of healthy adults, typically only causing PML in immunocompromised patients.

When patients are immunosuppressed – for organ transplantation, as a consequence of HIV infection, or by treatment with drugs such as TYSABRI® (natalizumab – Biogen Idec) or RITUXAN® (rituximab - Genentech) that dampen the host immune response – the JC virus may multiply unchecked and cause PML. These observations suggest that the immune system is important in regulating the asymptomatic nature of human JC virus infections.

The factors leading to activation of the latent infection are not fully understood, though abnormalities in T-cells may be important for reactivation and PML. PML has been reported in the published literature in HIV-positive patients, as well as immunosuppressed cancer patients (including patients with hematologic malignancies), organ transplant recipients, and patients with autoimmune diseases. There are no known interventions that can reliably prevent or adequately treat PML.

About Recombinant Human 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.

Clinical trials conducted on more than 160 patients in Europe, North America, South Africa 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, HCV, HBV, post-BMT and cancer. Additional studies include a NIAID/NIH-sponsored trial in idiopathic CD4 lymphocytopenia (ICL) and a cancer vaccine study in children with Ewing's sarcoma family of tumors or similar genetic tumors sponsored by US National Cancer Institute.

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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