

Cytheris, ImmunID Technologies and the Centre Léon Bérard announce the start of DivRescue, a collaborative R&D project principally funded by the 11th FUI call for projects (Interministries fund)

The DivRescue project aims to develop a new protocol for cancer patient management, evaluating immune status and, when necessary, stimulating immune reconstitution. This world-first relies on the synergy between the three main actors: two biotechnology companies ImmunID Technologies and Cytheris – leaders in immunology, diagnostics and pharmacy – and the Centre Léon Bérard, a pioneer in research into cancer-related immunosuppression. The project is accredited by competitiveness clusters Medicen Paris Region and Lyonbiopole as part of the 11th FUI call for projects (Interministries fund). It offers an integrated approach to patient management with the aim of increasing survival rates for immune-depressed patients. Starting with metastatic breast cancer, the study will soon be extended to management of other solid metastatic cancers.

Paris, Grenoble, Lyon (France) – 31 May 2011 – Cytheris, a biopharmaceutical company based in Paris – expert in development of new therapies for immune modulation, in particular based on interleukin-7; ImmunID Technologies, the Grenoble-based start-up – specialists in immune status monitoring, creators of the divpenia concept, which is currently being clinically tested. Divpenia is a new biomarker, indicator of the immune system's aptitude to provide optimal protection; and the Centre Léon Bérard in Lyon, a cancer treatment centre – pioneer in research into cancer-related immunosuppression – announce the start of the DivRescue project. This project aims to integrate into cancer management an assessment of immune status and, in selected patients, reconstitution of defenses weakened by the disease and treatment. It is hoped that this theranostic approach will increase patient survival, in particular for patients with poor prognosis. This will be a world-first.

The project, coordinated by Cytheris, combines the fields of expertise of the three partners. While the two biotechnology companies are leaders in their respective fields, ImmunID in diagnostics and Cytheris in therapeutic applications of cytokines; the Lyon-based Cancer treatment centre houses two experts who have been interested in the contribution of the immune response to progression and prognosis in cancer for many years: Jean-Yves Blay, oncologist – professor at Université Claude Bernard, president of EORTC (European Organization for Research and Treatment of Cancer) – and Dr. Christophe Caux, immunologist. The Consortium is an indication of the partners' desire to combine their skills to provide the DivRescue project with a unique level of expertise in an immunological approach to cancer.

"Cytheris is delighted to be able to test the benefits of interleukin-7 in this global approach to treating the immune deficit in cancer patients. All the tools and competencies are in place to show the therapeutic benefit that will result from this type of disease management." indicates **Dr. Michel Morre, CEO of Cytheris**.

"DivRescue is part of a personalized medicine approach. Its aim is to identify divpenic patients presenting low immune defenses, and to provide them with an effective immune-reconstitution treatment. Beyond the complementary fields of expertise of the three partners, we would like to highlight the support of the competitiveness clusters which has contributed to the creation of an environment from which new France-based diagnostic and therapeutic solutions are likely to emerge." comments **Dr. Nicolas Pasqual, CEO of ImmunID**.

"DivRescue is the culmination of a program characterizing immunological disorders associated with tumor progression, initiated over 10 years ago at the Centre Léon Bérard. This is the start of therapeutic clinical applications." explains **Pr. Jean-Yves Blay, oncologist at the Centre de Lutte Contre le Cancer, Lyon**. "The first project allowed us to identify the prognostic value of lymphopenia for toxicity and survival in patients with evolving neoplastic disease. With DivRescue we will make our first attempt to correct T-lymphocyte numbers. We

will associate this with follow-up of repertoire diversity, as we have shown that alteration of this – Divpenia – is also a major prognostic factor, independent of lymphopenia."

DivRescue is accredited by two worldwide competitiveness clusters, Lyonbiopôle and Medicen.

"DivRescue is a world-first in theranostics. That ImmunID, board member representing SMBs at Lyonbiopole, is part of this project confirms the role of the cluster as a catalyst for innovation in the worldwide fight against infectious diseases and cancer, which are its domains of specialization." declares **Yves Laurent, General Manager of Lyonbiopole**.

"The DivRescue project is an indicator of the vitality of the Ile-de-France region in the identification of partners, and of the benefits that this type of group can provide. It combines high quality partners around key themes at the heart of our main interests: diagnosis, therapeutics and technology for health. We are delighted with this well-deserved success. The fact that Lyonbiopole and Medicen both accredited this project is a good example of the additional value their cooperation can provide to innovative projects." adds **François Chevillard, Deputy Manager of the Medicen Paris Region competitiveness cluster**.

At the heart of the DivRescue project there is a world-first: to be able to identify cancer patients with an increased risk of relapse and infection, and to offer them a treatment to reconstitute their immune system. This should significantly improve prognosis. The clinical interventions will be performed at the Centre Léon Bérard, a state-of-the-art hospital centre with a good patient recruitment capacity and a unique expertise in cancer immunology. Using the Multi-N-plex/ImmunTraCkeR technology designed by ImmunID, the project will use divpenia, a fine analysis of the immune potential of a patient, to identify patients with a profile combining lymphopenia and Divpenia (a low diversity of the lymphocyte repertoire). The work of Jean-Yves Blay and Christophe Caux has shown this to be an indicator of poor prognosis in patients with metastatic breast cancer. Patients presenting with lympho-divpenia will then be offered treatment with recombinant human interleukin-7 (CYT107), developed and produced by Cytheris. CYT107 can help stimulate lymphocyte production and induce reconstitution of immune diversity, in particular for CD4 and CD8 T-lymphocyte subsets. The impact of IL7 treatment on T-lymphocyte reconstitution (restoring lympho-divpenia) and on the specific immune response will be correlated with clinical benefit.

The project is expected to last three years. It should allow the partners to pursue the development of various immunological tools based on cellular, molecular and bio-informatic technologies; to adapt divpenia to the specific context of immune-reconstitution using CYT107, which targets CD4 and CD8 T-cell subsets; and to demonstrate that this strategy for immune-reconstitution leads to reduced toxicity, risk of infection and relapse, with a measurable impact on patient quality of life and survival. Other multi-centre studies will follow, with the Institut Gustave Roussy, Villejuif, as a privileged partner.

The Consortium will first investigate metastatic breast cancer, and will then extend studies to other solid metastatic cancers, in particular metastatic sarcomas and ovarian cancer.

The project has received €2.6 million funding from the 11th FUI call for R&D projects (Interministries Fund), managed by OSEO and the ERDF.

About divpenia - <http://divpenie.com/>

Divpenia is a diagnostic and prognostic biomarker currently being clinically validated. It measures the level of an individual's immune assets throughout their lives, and in particular during and after treatment. It is defined by ImmunID as a reduced lymphocyte diversity, which corresponds to a reduction in diversity of the T and B receptors. It is based on measurement of receptor diversity by the ImmunTraCkeR® or Immun'Ig® tests using a blood sample. These tests identify and characterize V(D)J rearrangements within genomic DNA. The diversity threshold expected for healthy, immune competent subjects is currently being defined. Below these levels, Divpenia is diagnosed. Clinical trials in patients with metastatic breast cancer have shown that a profile combining lymphopenia and Divpenia is an indicator of poor prognosis. Over 700 patients are included in various collaborative clinical trials initiated around the concept of divpenia.

About human recombinant Interleukin-7 (CYT107)

Recombinant human Interleukin-7 (CYT107) is a critical modulator for recovery and improvement of T-lymphocyte levels. As a growth factor and physiological cytokine produced by the thymus and other epithelia, Interleukin-7 (IL-7) plays an essential, and in some cases non-redundant, role in stimulating the development and expansion of T-lymphocytes, both within the thymus and at peripheral sites. Clinical trials carried out on over 180 patients in

Europe, North America, South Africa and Taiwan have shown IL-7 to be capable of stimulating and protecting CD4 and CD8 T-lymphocyte subsets.

About Cytheris - www.cytheris.com

Cytheris S.A. is a French biopharmaceutical company focused on research and development of new therapies for immune modulation. These drugs aim to reconstitute and enhance the activity of the immune system of patients with cancer, chronic viral or bacterial infections (e.g. HIV or hepatitis C) or who have received lympho-depleting treatments, chemotherapy, bone marrow or hematopoietic cell transplants. Founded in 1999, the company is based in the Paris area at Issy-les-Moulineaux and has a US subsidiary at Rockville (MD). Cytheris is currently involved in several international clinical trials to assess applications of IL-7 for the treatment of chronic viral infections (HIV, HCV, HBV), and as part of cancer treatment.

About ImmunID Technologies - www.immunid.com

Based in Grenoble, France, ImmunID Technologies is a molecular diagnostics company which uses a proprietary method to analyze immune repertoire diversity. Based on this, ImmunID develops and commercializes innovative tests and services to analyze immune status. In 2010 ImmunID introduced a new biomarker, divpenia®, an indicator of the extent of an individual's immune defenses, which provides more information than lymphocyte counting alone. This contributed to the concept of Divpenia®, defined as the clinical state of reduced lymphocyte diversity, a prognostic factor indicative of an increased risk of infection and mortality. Through its services, ImmunID contributes to the development of personalized medicine, in particular for the follow-up of patients receiving treatment based on monoclonal antibodies, interleukins or chemotherapy as part of cancer treatment (breast and lung cancer, leukemia and lymphoma), or for infectious diseases (HIV, HCV and septicemia). The company is a member of ADEBAG, Lyonbiopole and the CLARA Cancéropôle.

About the Centre Léon Bérard - www.centreleonberard.fr

Located in Lyon, the Centre Léon Bérard is a member of UNICANCER (which groups together all the cancer treatment centers in France) and the French federation of cancer treatment centers. This group unites 20 French hospitals whose main activity is treating cancer patients. The Centre Léon Bérard is a non-profit, private health establishment contributing to collective interests (ESPIC). It has three main aims: care, teaching and research in the field of cancer treatment. The Center treats 22,500 patients per year, from the Rhône-Alps region, France and abroad. Its vocation is to offer cancer patients access to high quality holistic clinical management and research innovations. To do so, 170 physicians interact with over 350 scientists in programs ranging from basic research right up to clinical applications. The Center has close collaborations with the Centre de Recherche en Cancérologie, Lyon, recognized as a center of excellence by the French Minister for education and research, and the Centre d'Essai Clinique de Phase Précoce (Early phase clinical trials center), which is accredited by the French National Institute for Cancer.

About the 11th FUI Call for projects

As part of this call for projects, 83 new collaborative research and development projects submitted by 52 competitiveness clusters will be awarded a combined €76 million funding by the French government through the FUI (Fonds unique interministériel, Interministries fund). Additional funding for most of these projects, from territorial groups and European Community funds (ERDF), contributes a further €56 million. The 83 projects awarded funding were selected from among 185 projects submitted, based on their innovative characteristics and the economic activity they are likely to generate.

Competitvity clusters: www.lyonbiopole.com www.medicen.org

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