



PRESS RELEASE
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FOR IMMEDIATE RELEASE

SOLUBLE LAG-3 PROTEIN IS A PROGNOSTIC FACTOR IN BREAST CANCER

Immutep S.A. announced today the publication of a research paper showing that soluble LAG-3 (Lymphocyte Activation Gene-3) protein (sLAG-3) is a prognostic indicator for survival in breast cancers expressing oestrogen or progesterone receptors. The results pave the way for the testing of a recombinant sLAG-3 protein as an adjuvant therapy for breast cancer in clinical trials.

The study (Cancer Letters 235 (2006) 147-153) was carried out by Dr Marie-France Pichon and Kamel Hacene of the René Huguenin Cancer Centre in Saint-Cloud, near Paris, and Pr. Frédéric Triebel when he was at the Pharmacy Faculty of University Paris 11. Dr Triebel is now Scientific and Medical Director of Immutep S.A.

In contrast to the long-held belief that breast cancer is a weakly immunogenic tumour, accumulating evidence indicates that an immune infiltrate is an invariable finding in breast cancers; raising hopes that immunotherapy may succeed in targeted patients, specifically those with either regional or minimal residual disease. However, no immunologically-related prognostic factor has yet been established that may help to define subsets of patients who are more prone to respond to immunotherapy. High levels of soluble LAG-3 protein (sLAG-3) in sera have previously been shown to be associated, as a Th1 marker, with resistance to tuberculosis in large series of patients. The researchers therefore hypothesized that, if cell-mediated immune mechanisms are indeed important for improved prognosis, high levels of sLAG-3 might be correlated with improved survival in some subsets of breast cancer patients. Studying a cohort of 246 patients' sera collected in 1994 at the time of first diagnosis, it was found that both disease-free and overall survival rates were higher in those patients with oestrogen or progesterone receptor positive tumour cells who had detectable levels of sLAG-3 at diagnosis than in patients with undetectable sLAG-3 levels. These results indicate that sLAG-3 may be a valuable marker for prognosis in some subsets of breast cancers and, more importantly, that cell-mediated mechanisms such as Th1 responses do have an impact on survival, a prerequisite before the setting up of immunotherapy protocols as a form of adjuvant therapy for breast cancer.

“These results shed new light on the importance of cellular immunity in breast cancer and warrant new efforts in using immunotherapy as an add-on to conventional chemotherapy in advanced breast cancer,” said Pr. Jean-Nicolas Munck, Director of the René Huguenin Cancer Centre whose Oncobiology Laboratory and Medical Statistics Service carried out the clinical part of the study.

The LAG-3 analyses were performed at the Pharmacy Faculty of University Paris 11. “It is striking that whatever the stage of the disease in 1994 and the type of subsequent therapy, we were able to show that high levels of sLAG-3 in the ng/ml range in the sera collected at diagnosis are associated with a much better outcome 10 years later,” said Frédéric Triebel. “These results have encouraged us to mimic nature’s work by directly injecting in patients a recombinant sLAG-3 protein, termed IMP321, without any tumour antigen, as a first line therapy in mostly incurable diseases such as metastatic renal cell or breast carcinomas.”

Soluble LAG-3 is a circulating form of LAG-3 derived by an alternative splicing event. LAG-3 was discovered by Frédéric Triebel and is key mediator of the immune system expressed on the surface of activated T cells. Immutep has an exclusive licence to the molecule and related applications.

Immutep and the René Huguenin Cancer Centre are planning to conduct clinical trials with the Company's sLAG-3 immunostimulatory factor, *ImmuFact*[®] IMP321, in conjunction with chemotherapy, later in the year. Apart from the research work and clinical trials discussed here, the René Huguenin Cancer Centre has no other links with Immutep and no member of its staff has a financial interest in the Company.

For further information please visit the web-site www.immutep.com or e-mail John Hawken, CEO, at JBHawken@immutep.com.

Notes to Editors

Immutep S.A.

Immutep S.A. is a biopharmaceutical company developing technologies for novel immunotherapies for the treatment of cancer and chronic infectious diseases and new approaches to immune response modulation. The Company's technologies are based on the properties of LAG-3. Immutep is developing its products both in-house and in partnership with pharmaceutical and biotech companies. The Company was formed in 2001 by Frédéric Triebel, the scientific founder, and John B. Hawken, a specialist in the management of biotech start-ups, and has its headquarters and research facilities near Paris, France. Immutep is backed by the Paris-based venture capital firm Innoven Partenaires and the venture capital fund H2I, a specialist Biotech fund managed by Unicorn Biotutors/Equitis (Paris).

The Technology

The Company's range of products is derived from LAG-3 (CD223), an immunomodulatory protein expressed on the surface of activated T cells. The three unique proprietary product platforms make use of the key roles played by this natural human protein in the regulation of the immune system.

***ImmuFact*[®] - T cell Immunostimulatory Factors for amplifying the T cell response**

The lead product, *ImmuFact*[®] IMP321, is a highly potent T cell immunostimulatory factor derived from the soluble form of LAG-3 that binds, with high affinity, to MHC class II molecules expressed by dendritic cells (DC). This binding leads to DC maturation, migration to the lymph nodes and enhanced cross-presentation of antigens to T cells. As a result, strong and sustained anti-tumour or anti-viral cytotoxic T cell responses are obtained when IMP321 is injected alone or in combination with antigens.

***ImmuCine*[®] – Immunostimulatory Vaccines**

The Company is developing a second technology that will make it possible to design novel therapeutic vaccines with even greater potency and efficacy. Covalently linking an antigen to IMP321 in a fusion protein results in both vectorisation of the antigen to the DC as well as the immunostimulatory effect described above. These dual action vaccines will be particularly useful in very difficult cases like HIV.

***ImmuTune*[®] – Fine Tuning of the Immune Response**

The third technology uses LAG-3-specific antibodies to control signalling of the membrane-bound LAG-3 molecule into activated effector T cells or regulatory T cells (Tregs) to modulate the T cell response.

Clinical Development (*ImmuFact*)

Immutep is completing two randomised single-blind escalating-dose Phase I studies in 108 healthy individuals with IMP321 alone and combined with two well-defined standard types of antigens: soluble influenza virus antigens and particulate hepatitis B surface antigen. The clinical phase of the first study in 60 subjects is complete and has shown good tolerability with no adverse events. A Phase I clinical trial in metastatic renal cell carcinoma started in September 2005 with IMP321 injected alone.

Centre René Huguenin de Lutte contre le Cancer

The René Huguenin Centre for the Fight against Cancer is a comprehensive cancer centre that treats more than 3,000 new cases of cancer each year, with more than 2,000 new cases of breast cancer. It has a medical staff of 66 practitioners. Besides participation in therapeutic trials, the Centre has developed expertise in the field of tumorigenesis and pharmacogenetics of breast cancers.

University Paris 11

University Paris 11 is one of the biggest French universities with a complete array of disciplines ranging from pure science to clinical practices in medicine and covering life and health sciences, law and economics. The development of the "Pharmatechnopole" in the Faculty of Pharmacy hosting new young innovative companies is one of the measures designed to improve its technology transfer capacity. (www.u-psud.fr)