



Immutep Reports that LAG-3 Enhances Activity of a Cellular Cancer Immunotherapy in Preclinical Studies

Research paper describes increase in potency of a GM-CSF-secreting tumor cell immunotherapy by a LAG-3 fusion protein immunopotentiator

Orsay, June 25, 2008 - Immutep S.A., a biopharmaceutical company specialized in immunostimulatory and immunomodulatory treatments of cancer and infectious or autoimmune disease, announced today the publication of research conducted by Cell Genesys, Inc. showing that a lymphocyte activation gene-3 fusion protein increases the potency of a granulocyte macrophage colony-stimulating factor (GM-CSF)-secreting tumor cell immunotherapy. These data were published in the June issue of *Clinical Cancer Research*.

The research team found that combining mLAG-3Ig with a murine GM-CSF-secreting tumor cell immunotherapy prolonged the survival of tumor-bearing animals compared to animals treated with either therapy alone. Prolonged survival correlated with increased numbers of systemic IFN γ -secreting CD8⁺ T-cells and a significantly increased infiltration of activated effector CD8⁺ T-cells into the tumor.

“Combination therapies are being evaluated with the goal of enhancing overall antitumor activity, which could allow treatment of patients with large tumor burden,” said Frédéric Triebel, Immutep's Scientific and Medical Director. “Elevated levels of TNF α were detected in the supernatant of splenocytes isolated from animals treated with the combination therapy compared to splenocytes from animals injected with the immunotherapy alone. This increased proinflammatory cytokine production that correlated with an overall enhancement of *in vivo* CD8 T-cell activation clearly indicates that LAG-3 further increases anti-tumor activity in conditions where GM-CSF is already used as an immunostimulant.”

The mLAG-3Ig fusion protein is a murine homologue of Immutep's lead product *ImmuFact*[®] IMP321, a potent natural human immunostimulatory factor designed to amplify the T cell immune response. IMP321 can be used either as an immunopotentiator in therapeutic vaccines or alone at higher doses as a monotherapy or in combination with chemotherapy. Six clinical trials have been initiated with *ImmuFact* IMP321 in the last three years.

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

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Notes to Editors

The Published Paper

“Lymphocyte Activation Gene-3 Fusion Protein Increases the Potency of a Granulocyte Macrophage Colony-Stimulating Factor-Secreting Tumor Cell Immunotherapy”, Betty Li, Melinda VanRoey, Frédéric Triebel and Karin Jooss, *Clinical Cancer Research* 2008; 14(11) June 1, 2008.

Immutep S.A.

Immutep S.A. is a biopharmaceutical company developing immunostimulatory factors for the treatment of cancer and chronic infectious diseases and immunomodulatory therapeutic antibodies for the treatment of cancer or autoimmune disease. The Company's technologies are based on the LAG-3 immune control mechanism that mediates T cell immune responses.

The LAG-3 immune control mechanism

The lymphocyte activation gene-3 (LAG-3 or CD223) protein binds to the MHC class II molecule which is at the center of immune response induction. The LAG-3 immune control mechanism plays a role in the upregulation of the immune system through the activation of MHC class II⁺ antigen presenting cells like dendritic cells and monocytes (the primary target cells for IMP321) leading to the expansion of activated CD8 T cells (the secondary target cells).

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

The lead product, ImmuFact[®] IMP321, is a highly potent T cell immunostimulatory factor. It is a soluble form of LAG-3 that binds, with high affinity, to MHC class II molecules expressed by dendritic cells (DC) and monocytes. 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-tumor or anti-viral cytotoxic T cell responses are obtained.

IMP321 is currently being tested by a wide range of therapeutic vaccine companies as an adjuvant (low dose IMP321 mixed with an antigen) combined with their proprietary technologies.

Clinical Development

Immutep has completed two randomized single-blind escalating-dose Phase I studies in 108 healthy individuals with IMP321 alone and combined with two well-defined standard types of antigens to show safety of the product alone and as an adjuvant in therapeutic vaccines. Four new Phase I/II clinical trials are in progress: a clinical trial in metastatic renal cell carcinoma with IMP321 injected alone, a study in metastatic breast cancer combining IMP321 with paclitaxel in a chemo-immunotherapy protocol, a disease-free melanoma study with IMP321 as an adjuvant to peptide antigens and a lympho-depletive/adoptive transfer metastatic melanoma study.