



Immutep and GlaxoSmithKline sign licence agreement for IMP731, a novel therapeutic antibody for the treatment of autoimmune diseases

Worldwide licence gives GSK exclusive rights to depleting LAG-3 antibodies including *ImmuTune* IMP731

Orsay, France, January, 6th, 2010 - Immutep S.A. announced today the execution of a licence agreement granting GSK exclusive worldwide rights to *ImmuTune*[®] IMP731 and any other antibodies that deplete LAG-3 positive cells. IMP731 has demonstrated potency at low doses in preclinical models of T cell mediated inflammation and could represent a new therapeutic approach to the treatment of autoimmune disease.

Under the terms of the agreement, GSK will assume all development responsibility and associated costs for IMP731. Immutep will receive an upfront payment and milestones of up to £64 million (\$100 million) and is eligible for single-digit, tiered royalties if all objectives are achieved.

"We are very pleased to hand over the development of IMP731 to GSK, with its commitment to bringing breakthrough therapies to patients," said John Hawken, CEO. "For Immutep, the value created through this transaction will enable us to focus our resources on advancing our oncology assets, IMP321 and IMP701. IMP321 is ready for a Phase IIb/III trial in the chemo-immunotherapy of first-line metastatic cancer."

IMP731 is a cytotoxic antibody that depletes activated T cells. Chronically activated T cells are a major component in many autoimmune diseases. LAG-3 (Lymphocyte Activation Gene-3) is a marker for activated long-lived effector-memory T cells. Deleting activated pathogenic T cells rather than simply blocking one of their functions (for example production of TNF- α , IL-6, IL-23) is a new therapeutic approach.

In addition, selective depletion of these pathogenic LAG-3⁺ T cells will lead to targeted immunosuppression (i.e. only a subset of activated T cells will be suppressed, not all T cells as with corticoids or cyclosporin). This very specific long-lived immunosuppression should lead to higher therapeutic indices compared to classical immunosuppressive agents, with a reduced risk of increased susceptibility to infectious agents, as the pool of resting LAG-3 negative T cells will be left untouched.

Overall, such a targeted therapy, inducing long-term effects with a minimum number of injections is a promising approach in the many autoimmune diseases where self-antigens have activated T cells, for example, rheumatoid arthritis and multiple sclerosis.

Cabinet Luc Barny acted as legal advisor to Immutep.

For further information please visit the web-site www.immutep.com.

Notes to Editors

ImmuTune® IMP731 – depleting antibody

Lymphocyte-Activation Gene-3 (LAG-3, CD223) is a marker for recently activated effector T cells. During inflammation LAG-3 is strongly upregulated and plays an important role in antigen-presenting cell (APC) activation. Relatively few molecules have been identified as sustained *in vivo* T cell activation markers in human. IMP731 is an IgG1 antibody specific for the LAG-3 antigen, which has been shown to deplete LAG-3 positive cells by antibody mediated cell mediated cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC).

Activated T cells and autoimmune disease

Activated T lymphocytes are of major importance in many autoimmune diseases. Therefore specifically depleting LAG-3⁺ T cells will lead to targeted immunosuppression that will spare resting T cells while eliminating pathogenic activated T cells. It has previously been shown that anti-LAG-3 depleting antibodies inhibit heart allograft rejection in rats (Haudebourg et al, Transplantation 2007). In a second study, a cytotoxic LAG-3 chimeric antibody (IMP731) was shown to be a selective therapeutic depleting agent in a non-human primate model of T cell mediated inflammation. Depletion of LAG-3⁺ T lymphocytes resulted in a long-lasting inhibition of immune responses.

These preclinical studies were carried out in collaboration with Bernard Vanhove and Gilles Blancho's teams in the Inserm unit U643 at the University of Nantes, France

Selectively deleting activated T lymphocytes represents a promising therapeutic approach as an alternative to current immunosuppressive treatments in autoimmunity providing a competitive advantage by targeting only pathogenic T cells that are specific for auto- or allo-antigens without modifying the protective immunity directed against third party antigens

Inserm U643

The INSERM UMR 643 is hosted in the ITUN (Institut de Transplantation, Urologie, Néphrologie) at the Nantes University Hospital. The area of research of INSERM UMR 643 covers transplantation science and immunosuppression/tolerance. The aim is to analyze and inhibit immune responses mainly in organ and cellular transplantation. Immune-mediated kidney diseases, autoimmune diseases and gene therapy in which immune responses are of prime importance are also investigated.

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. Apart from the depleting antibody, IMP731, described above, two of the Company's other products are:

ImmuFact® IMP321

IMP321 is an APC (antigen presenting cell) activator that has completed a Phase I/II clinical trial combined with chemotherapy (chemo-immunotherapy) in first-line metastatic breast cancer. The trial showed a doubling of the clinical response rate compared to paclitaxel alone and a correlation with patient monocyte counts. Three Phase I/II clinical trials are in progress: in pancreatic cancer combining IMP321 with gemcitabine in chemoimmunotherapy, a disease-free melanoma study with IMP321 as a therapeutic vaccine adjuvant to peptide antigens and a lympho-depletive/adoptive transfer metastatic melanoma study.

ImmuTune® IMP701

IMP701 is an antagonist anti-LAG-3 antibody. It gives rise to T cell proliferation in a similar manner to anti-CTLA-4 and anti-PD-1 antibodies. The development of a human version for clinical trials is in progress.