



Immutep Announces Start of Clinical Trial in Pancreatic Cancer

A Phase I clinical trial of ImmuFact IMP321 in pancreatic cancer has started at Washington University in Saint Louis (MO)

Orsay, April 15, 2009 - Immutep S.A. announced today the first administration of IMP321 in pancreatic cancer patients in a Phase I trial conducted by Dr. William G. Hawkins at the Washington University School of Medicine in Saint Louis (MO).

IMP321 is a first-in-class immunopotentiator that stimulates antigen-presenting cells (APC), such as dendritic cells and monocytes, leading to markedly improved cytotoxic CD8 T cells responses against tumours in patients. The pancreatic cancer trial follows the promising results obtained in metastatic breast cancer with a similar chemo-immunotherapy protocol.

The phase I study is an open-label, two-arm, dose escalation trial in advanced pancreatic cancer treated by first-line gemcitabine alone or associated with increasing doses of IMP321 (3, 6.5, 13 and 26 mg). Investigators will assess the safety and tolerability of this new chemo-immunotherapy combination. The other points to be studied include IMP321's pharmacokinetics, pharmacodynamics, immunogenicity, a preliminary assessment of anti-tumour activity as well as the exploration of the molecule's mechanism of action. IMP321 will be given s.c. q14 for a 6-month period the day after gemcitabine administration, with an option for additional months of therapy if disease improvement or stabilisation is observed. Approximately 33 patients are expected to be enrolled.

"We are very pleased to start this trial in advanced pancreatic cancer patients which should provide information about the potency of IMP321 as an add-on immunostimulant for the induction of CD8 T cell responses in our patients," said William G. Hawkins, Principal Investigator and sponsor of this study. "Cancer of the pancreas carries an ominous prognosis and progress would not be possible without the valuable support and collaboration provided by the Gateway for Cancer Research, Immutep and the Siteman Cancer Center."

"Several new trials have started recently in chemo-immunotherapy," said Frédéric Triebel, Scientific & Medical Director of Immutep. "We believe that combining chemotherapy with immunotherapy could make a major contribution to improving chemotherapy outcomes in patients with a good immune status such as in first-line regimens."

Immutep's lead product is 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. Seven clinical trials have been initiated with ImmuFact IMP321 in the last four years.

"Our positive results in chemo-immunotherapy have encouraged us to engage in discussions with potential partners over Immutep's plans for IMP321," added John Hawken, CEO.

For further information please visit the web-site www.immutep.com. Patients interested in joining the pre-screening process for participating in the trial should contact the Siteman Cancer Center on +1 877 251 6485 (toll free in US) or +1 314 747 3046.

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Notes to Editors

The Washington University School of Medicine, Saint Louis, MO

Washington University School of Medicine's 2,100 employed and volunteer faculty physicians also are the medical staff of Barnes-Jewish and St. Louis Children's hospitals. The School of Medicine is one of the leading medical research, teaching and patient care institutions in the nation, currently ranked third in the nation by *U.S. News & World Report*. Through its affiliations with Barnes-Jewish and St. Louis Children's hospitals, the School of Medicine is linked to BJC HealthCare.

Dr William G. Hawkins

Dr Hawkins is the Assistant Professor of Surgery in the Hepatobiliary Pancreatic and Gastrointestinal Surgery Section. His specialty areas are complex cancer surgery for primary and metastatic lesions of the liver, pancreas and stomach and surgical management of soft-tissue sarcomas of the abdomen and extremities. He was educated at the State University of New York Medical School at Stony Brook followed by a Surgical Research Fellowship at Memorial Sloan-Kettering Cancer Center New York, N.Y., residency at Massachusetts General Hospital, and a Surgical Oncology Fellowship at Memorial Sloan-Kettering Cancer Center, New York, N.Y.

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 centre of immune response induction. LAG-3 is a two-way signalling molecule that 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 leading to the expansion of activated CD8 T cells, and
- the *downregulation* of the T cell response through signalling in T cells, both effector T cells and regulatory T 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-tumour or anti-viral cytotoxic T cell responses are obtained.

ImmuFact[®] - Clinical Development

Immutep has completed two randomised single-blind escalating-dose Phase I studies in 108 healthy individuals with IMP321 alone or combined with two well-defined standard types of antigens to show safety of the product alone and as an adjuvant in therapeutic vaccines. A safety trial in metastatic renal cell carcinoma with IMP321 injected alone has also been completed. Four new Phase I/II clinical trials are in progress: in metastatic breast cancer combining IMP321 with paclitaxel in a chemo-immunotherapy protocol, a disease-free melanoma study with IMP321 as a therapeutic vaccine adjuvant to peptide antigens, a lympho-depletive/adoptive transfer metastatic melanoma study and in pancreatic cancer combining IMP321 with gemcitabine in a chemo-immunotherapy protocol. More than 500 s.c. injections of IMP321 have been administered to date in Europe at doses up to 30 mg with no clinically significant drug-related adverse events.

ImmuTune[®] - Therapeutic antibodies

Immutep's second product candidate is ImmuTune IMP731, a cytotoxic antibody for depleting activated T cells in autoimmune disease. The Company is also developing IMP701, an antagonist antibody designed to increase T cell proliferation against cancer and infectious disease.