Immutep announces final results in phase I/II chemoimmunotherapy trial in metastatic breast cancer

Clinical research paper describes IMP321's potency in achieving clinical benefit in 90 per cent of patients, combined with paclitaxel in first-line metastatic breast cancer

Orsay, France, September 7, 2010 - Immutep S.A. announced today the publication of a clinical research paper showing that its lead product, IMP321, given with first-line paclitaxel achieved clinical benefit in 90 per cent of metastatic breast carcinoma (MBC) patients. Correlations were observed with both the patients' monocyte (i.e. the primary target cell for IMP321) count before treatment and the degree of activation of monocytes during treatment.

The study was an open-label fixed-dose-escalation trial carried out in three cancer centers in the Paris region. The lead center was the René Huguenin Cancer Centre in Saint Cloud. The other centers were Tenon Hospital and the Georges Pompidou European Hospital in Paris. The immuno-monitoring was done by Immutep at its laboratories near Paris.

MBC patients were administered one dose of IMP321 s.c. every two weeks for a total of 24 weeks (12 injections). The repeated single doses were administered the day after chemotherapy at day 2 and day 16 of the 28-day cycles of paclitaxel (6 cycles). Blood samples were taken 13 days after the sixth and the twelfth IMP321 injections to determine sustained APC, NK and memory CD8 T cell responses. Thirty patients received IMP321 in three cohorts (doses: 0.25, 1.25 and 6.25 mg).

IMP321 induced both a sustained increase in the number and activation of APC (monocytes and dendritic cells) and an increase in the percentage of NK and long-lived cytotoxic effector-memory CD8 T cells. Clinical benefit was observed for 90 per cent of patients with only 3 progressors at 6 months. Also, the objective tumor response rate of 50 per cent compared favorably to the 25 per cent rate reported in the historical control group.

IMP321 is a recombinant soluble LAG-3Ig fusion protein that binds to MHC class II with high avidity and mediates APC and then antigen-experienced memory $CD8^+$ T cell activation. Further evidence of the mechanism of action came from the analysis of tumor regression during the second 3 months compared to the first 3 months. Under chemo alone, most tumor regression takes place during the early period and less during the later period. Using IMP321, however, investigators observed enhanced tumor regression in the later period as well; late responses are characteristic of a cancer immunotherapy effect.

“I was very pleased to be able to present these results in an oral presentation at ASCO in June,” said Dr Maya Gutierrez, Principal Investigator, René Huguenin Cancer Centre.

“We now have the results required to go forward to a pivotal trial,” said Frédéric Triebel, Scientific & Medical Director of Immutep. “This form of chemo-immunotherapy should be applicable to many chemotherapies. For example, it is now being tested in the USA in association with gemcitabine in pancreatic cancer."

“Partnering discussions are in progress to carry out the Phase IIb/III pivotal trial leading to Conditional Marketing Authorisation in Europe and further trials in other cancers and with other chemotherapies,” added John Hawken, CEO.

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

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Notes to Editors

The published paper

"First-line Chemoimmunotherapy in Metastatic Breast Carcinoma: Combination of Paclitaxel and IMP321 (LAG-3Ig) Enhances Immune Responses and Antitumor Activity", Chrystelle Brignone, Maya Gutierrez, Fawzia Mefti, Etienne Brain, Rosana Jarcau, Frédérique Cvitkovic, Nabil Bousetta, Jacques Medioni, Joseph Gligorov, Caroline Grygar, Manon Marcu and Frédéric Triebel, Journal of Translational Medecine, 8:71 2010.

Immu*Fact*® - T cell Immunostimulatory Agent for amplifying the T cell response

Immu*Fact*® IMP321 is a first-in-class antigen-presenting cell (APC) agonist. It is a soluble form of the LAG-3 ("lymphocyte activation gene-3") T cell surface receptor that binds, with high affinity, to MHC ("major histocompatibility complex") class II molecules on APC such as monocytes and dendritic cells. Repeated IMP321 injections lead to strong anti-tumor CD8 T cell responses in cancer patients especially in combination with chemotherapy.

Metastatic Breast Cancer and Chemoimmunotherapy

Metastatic breast cancer remains incurable. The failure of current approaches is generally attributed to the outgrowth of breast tumor cells that are inherently resistant to standard treatments. Manipulating the immune system to recognize and eradicate breast tumor cells is a highly attractive alternative approach to disease management. Active immunization offers multiple theoretical advantages over all other therapies, including low toxicity. The sustained antitumor effect due to *immunological memory* would obviate the requirement for prolonged, repetitive cycles of therapy.

The objective of chemoimmunotherapy is to amplify *natural pre-existing* T cell responses specific for any known or unknown tumor antigen and to recruit and amplify *new* tumor-specific T cell responses resulting from the use of cytotoxic drugs. The direct cytolytic effect of some cytotoxic drugs, such as paclitaxel, can enhance antigen presentation by inducing tumor cell apoptosis. This mechanism of therapeutic synergy has been shown with cyclophosphamide, doxorubicin, or paclitaxel when given with dendritic cell–based vaccines. Until 9 years ago, it was thought that the T cell depletion caused by chemotherapy would make immunotherapy ineffective. However it has now been shown that, on the contrary, the vigorous T cell repopulation following depletion can be directed against the tumor.

Soluble LAG-3 protein is a prognostic factor in breast cancer

Immu*Fact* IMP321 is closely related to the soluble form of the LAG-3 protein which is a prognostic indicator for survival in breast cancers expressing estrogen or progesterone receptors. This was shown in a study carried out by researchers at the René Huguenin Cancer Centre and Pr. Frédéric Triebel when he was at the Pharmacy Faculty of University Paris 11. These results paved the way for the current clinical trial. (Immutep Press Release No 6, April 2006)

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 special expertise in the field of tumorigenesis and pharmacogenetics of breast cancers. Professor Jean-Nicolas Munck is the Directeur-Général.

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.

Immu*Fact*® - Clinical Development

More than 600 s.c. injections of IMP321 have been administered to date in Europe and the USA at doses up to 30 mg with no clinically significant drug-related adverse events. A Phase I trial in metastatic renal cell carcinoma with IMP321 alone has been completed. A Phase I/II trial in metastatic breast cancer combining IMP321 with weekly paclitaxel in a chemo-immunotherapy protocol has been completed (http://clinicaltrials.gov/ct/gui/show/NCT00349934?order=1). Three Phase I/II clinical trials are in progress: in pancreatic cancer combining IMP321 with gemcitabine in chemoimmunotherapy (http://www.clinicaltrials.gov/ct2/show/NCT00732082?term=07-0265&rank=1), a disease-free melanoma study with IMP321 as a therapeutic vaccine adjuvant to peptide antigens and a lympho-depletive/adoptive transfer metastatic melanoma study.