



Immutep

**IMMUTEP ANNOUNCES POSITIVE INTERIM RESULTS FROM A STUDY OF IMMUFAC<sup>®</sup> IMP321 IN METASTATIC BREAST CANCER**

***Study shows strong increases of monocytes and CD8<sup>+</sup> T cells and associated clinical responses***

**Orsay, November 28, 2007** - Immutep S.A announced positive interim results from a Phase I/II study of its lead product, ImmuFact<sup>®</sup> IMP321 in patients with metastatic breast cancer (MBC). The data were presented at the 22<sup>nd</sup> annual meeting of the International Society for Biological Therapy of Cancer (ISBTc) in Boston.

ImmuFact<sup>®</sup> IMP321 is a potent natural human immunostimulatory factor designed to amplify the T cell immune response. It can be used either as an immunopotentiator in therapeutic vaccines or alone at higher doses as a monotherapy or in chemo-immunotherapy. Six clinical trials have been initiated with ImmuFact IMP321 in the last 30 months.

The clinical trial is an open-label dose-escalation study of IMP321 given the day after paclitaxel (chemo-immunotherapy). In the first cohort of eight patients, the study showed strong increases in the number of monocytes and CD8<sup>+</sup> T cells and associated clinical responses.

This trial highlights the potential of IMP321 as a complementary immunotherapy to chemotherapy. The rationale for chemo-immunotherapy is that the *chemotherapy* causes apoptosis of tumour cells which releases antigens for several days. These antigens are taken up by the dendritic cell/monocyte network, the so-called antigen-presenting cells (APCs), leading to an immune response against them. By injecting an *immunostimulant*, especially an APC activator like IMP321, one can boost the network in order to increase the numbers of activated monocytes and CD8 T cells, both of which are endowed with anti-tumour activity.

The clinical trial is being conducted at the René Huguenin Cancer Centre, Saint Cloud, near Paris. The Principal Investigator is Dr Maya Gutierrez. It is an open-label fixed dose-escalation Phase I/II study, performed in an ambulatory setting in patients receiving as a first-line chemotherapy for MBC the standard six cycles of weekly paclitaxel (80 mg/m<sup>2</sup> at D1, D8 and D15 of a 4-week cycle). Two IMP321 doses, 0.25 and 1.25 mg given s.c., are being tested, given at D2 and D16 of this 4-week cycle, for six courses.

“Concurrent chemo-immunotherapy is a promising cancer treatment. Some preclinical and also clinical studies have shown that immunotherapy can enhance anti tumour activity of chemotherapy,” said Dr Gutierrez. “In metastatic breast cancer, taxane-based chemotherapy is considered as the gold standard first line in patients previously treated with anthracyclines in adjuvant setting. Weekly paclitaxel is generally well tolerated and is considered to have a better therapeutic index than 3 weeks administration. Mechanisms of action combine mitotic arrest, anti-angiogenic and pro-apoptotic effects.”

The first cohort of eight patients (0.25 mg) showed that IMP321 was very well tolerated with a good efficacy profile. The clinical responses were six tumour regressions and one disease stabilization out of eight patients, to be compared to a 35 per cent response rate with chemotherapy alone. A three-fold increase in activated MHC class II<sup>+</sup> monocyte blood counts and a two-fold increase in activated CD8<sup>+</sup> circulating T cells were observed two weeks after the last injection in patients. Both these effects obtained *in vivo* mimic the *in vitro* effect of IMP321 on human peripheral blood mononuclear cells (see press release September 17, 2007).

“I am encouraged that such important systemic effects on both the innate (monocytes) and the adaptive (CD8 T cells) arms of the immune response could be obtained with a dose as low as a quarter of a mg,” said Frédéric Triebel, Immutep's Scientific and Medical Director. “This is

probably related to the longer protocol we are using now, incorporating 12 injections administered over six months. In fact, similar effects were previously seen in metastatic renal cell carcinoma patients (results also reported at the iSBTc meeting) with a higher dose of the product (6.25 mg) but given only six times over three months. Building-up a strong and multi-faceted anti-tumour response safely over six months or even longer in patients receiving first-line chemotherapy is the ultimate goal for IMP321. It has repeatedly been shown that cellular immunity of this type is an essential component for long-term survival.”

For further information please visit the web-site [www.immutep.com](http://www.immutep.com) or e-mail John Hawken, CEO, at [JBHawken@immutep.com](mailto:JBHawken@immutep.com).

Notes to Editors

### **Metastatic Breast Cancer and Chemo-immunotherapy**

Metastatic breast cancer remains incurable. The failure of current approaches is generally attributed to the outgrowth of breast tumour cells that are inherently resistant to standard treatments. Manipulating the immune system to recognize and eradicate breast tumour cells is a highly attractive alternative approach to disease management and could be associated with chemotherapy (chemo-immunotherapy) to increase response rates and survival.

The objective of the immunotherapy is to amplify *natural pre-existing* APCs and T cell responses specific for any known or unknown tumour antigens and also to recruit and amplify *new* tumour-specific T cell responses occurring during a chemotherapy cycle. The direct cytolytic effect of some cytotoxic drugs, such as paclitaxel, can enhance antigen availability by inducing tumour cell apoptosis. Until 5 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 tumour, the so-called "rebound" effect.

### **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, including more than 2,000 new cases of breast cancer. It has a medical staff of 66 practitioners. Besides participating 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 of the Centre.

### **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. The LAG-3 immune control mechanism plays a role in the upregulation of the immune system through the activation of MHC class II<sup>+</sup> 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).

### **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.

### **ImmuFact<sup>®</sup> - T cell Immunostimulatory Factors for amplifying the T cell response**

The lead product, ImmuFact<sup>®</sup> 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.

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