ASX/Media Release

Immutep doses First Patient in TACTI-002 Phase II Trial

- The First Patient has been dosed at "START Madrid- FJD" in Spain
- Clinical trial sites are active and more will be activated and commence recruitment in coming months

SYDNEY, AUSTRALIA – March 6, 2019 – Immutep Limited (ASX: IMM; NASDAQ: IMMP) ("Immutep" or "the Company"), announces the first patient has been dosed with the combination of Keytruda® and efti for TACTI-002, a Phase II clinical study.

TACTI-002 (Two ACTive Immunotherapies) is being conducted in collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada). The study will evaluate the combination of Immutep's lead product candidate eftilagimod alpha ("efti" or "IMP321") with MSD's KEYTRUDA® (or pembrolizumab, a PD-1 blocking antibody) in up to 109 patients with second line head and neck squamous cell carcinoma or non-small cell lung cancer in first and second line. The study will take place in up to 13 study centres across the U.S., Europe and Australia.

Recruitment for the trial commenced at 2 sites in Australia, 1 site in the US, 4 sites in Europe. Four further clinical trial sites are expected to initiate and commence recruitment in the coming months.

Immutep CSO and CMO, Dr Frederic Triebel, said: "Dosing the first patient of our TACTI-002 Phase II clinical study is an important milestone. The interim data reported so far from our TACTI-mel Phase I study in melanoma has shown that the combination of efti with pembrolizumab, a PD-1 blocking antibody, is delivering long lasting and durable responses. Given that the TACTI-002 study leverages the same combination therapy, we are hopeful that it will be beneficial for patients with head and neck squamous cell carcinoma or non-small cell lung cancer."

About the TACTI-002 clinical trial

Title of Study	TACTI-002 (Two ACTive Immunotherapeutics): A Multicenter, Open Label, Phase II Study in Patients with Previously Untreated Unresectable or Metastatic Non-small Cell Lung Cancer (NSCLC), or Recurrent PD-X Refractory NSCLC or With Recurrent or Metastatic Squamous Head and Neck Cancer (HNSCC) Receiving the Soluble LAG-3 Fusion Protein Eftilagimod Alpha (IMP321) in Combination with Pembrolizumab (PD-1 Antagonist)
ClinicalTrials.gov Identifier	NCT03625323
Objectives	**Primary Objective** • Evaluation of objective response rate (ORR) according to iRECIST **Key Secondary Objectives** • Safety and tolerability of the combination • Response rate according to RECIST 1.1 • Disease control rate according to iRECIST and RECIST 1.1 • Progression free survival (PFS) • Overall survival (OS)

	• Pharmacokinetic and immunogenicity profile of eftilagimod alpha
Study Design	
Planned Sample Size	Up to 109 patients
Study Population	**Key inclusion criteria** 1. Part A (1st line, PD-X naïve NSCLC): histologically- or cytologically-confirmed diagnosis of non-small cell lung carcinoma stage IIIB not amenable to curative treatment or stage IV not amenable to EGFR/ALK based therapy, treatment naïve for systemic therapy given for advanced/metastatic disease (previous palliative radiotherapy for advanced/metastatic disease acceptable) Part B (2nd line, PD-X refractory NSCLC): histologically- or cytologically-confirmed diagnosis of NSCLC after failure of first-line treatment (for metastatic disease) with at least 2 cycles of any PD-1/PD-L1 containing based therapy (i.e. nivolumab, pembrolizumab, avelumab, durvulumab, etc) alone, or in combination with any other immunotherapeutic or chemotherapy. Part C (2nd line PD-X naive HNSCC): Histologically- or cytologically-confirmed recurrent disease not amenable to curative treatment with local or systemic therapy, or metastatic (disseminated) HNSCC of the oral cavity, oropharynx, hypopharynx, and larynx that is considered incurable by local therapies after failure of prior platinum-based therapy. 2. Submission of formalin-fixed diagnostic tumor tissue 3. ECOG performance status 0-1. 4. Expected survival > 3 months. **Key exclusion criteria** 1. For part A (1st line, PD-X naïve NSCLC): • The NSCLC can be treated with curative intent with either surgical resection and/or chemoradiation and/or radiation. • Has received systemic therapy for the treatment of their stage IV NSCLC. Completion of treatment with chemotherapy and/or radiation as part of neoadjuvant/adjuvant therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of metastatic disease. • EGFR-sensitizing mutation and/or is EML4 gene/ ALK gene fusion positive (ALK translocation). For Part B (2nd line, PD-X refractory NSCLC): • Symptomatic ascites or pleural effusion. • > 1 line of chemotherapy for metastatic disease. For Part C (2nd line PD-X naive HNSCC): • Disease is suitable for local therapy administered with curative intent. • Previously treated with > 1 systemic regimens for recurrent and/or metastatic disease. 2. Prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways) (Part A and C only)

3. Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti PD L2 agent or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g., CTLA-4, OX 40, CD137) and was discontinued from that treatment due to a Grade 3 or higher irAE (Part B only)
4. Has received prior chemotherapy, anti-cancer monoclonal antibody, major surgery, another systemic cancer therapy or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to cycle 1 day 1.
   Note: Patients must have recovered from all AEs due to previous therapies to ≤Grade 1 or baseline. Patients with ≤Grade 2 neuropathy, alopecia and elevated transaminases in case of liver metastases may be eligible. If patient received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment. Participants who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks after the last dose of the previous investigational agent.
5. Known active central nervous system metastasis and/or carcinomatous meningitis. Patients with previously treated brain metastases may participate provided they are radiologically stable: i.e. without evidence of progression for at least 4 weeks by repeat imaging, clinically stable and without requirement for steroid treatment for at least 14 days prior to cycle 1 day 1.
6. Receives continuous systemic treatment with either corticosteroids (>10 mg daily prednisone equivalents) or other immunosuppressive medications within 7 days prior to cycle 1 day 1. Inhaled or topical steroids and physiological replacement doses of up to 10 mg daily prednisone equivalents are permitted in the absence of active auto-immune disease.

About Immutep

Immutep is a globally active biotechnology company that is a leader in the development of immunotherapeutic products for the treatment of cancer and autoimmune disease. Immutep is dedicated to leveraging its technology and expertise to bring innovative treatment options to market for patients and to maximize value to shareholders. Immutep is listed on the Australian Securities Exchange (IMM), and on the NASDAQ (IMMP) in the United States.

Immutep's current lead product candidate is eftilagimod alpha ("efti" or "IMP321"), a soluble LAG-3Ig fusion protein based on the LAG-3 immune control mechanism. This mechanism plays a vital role in the regulation of the T cell immune response. Efti is currently in a Phase IIb clinical trial as a chemoimmunotherapy for metastatic breast cancer termed AIPAC (clinicaltrials.gov identifier NCT02614833); a Phase II clinical trial referred to as TACTI-002 (Two ACTive Immunotherapies) to evaluate a combination of efti with KEYTRUDA® (pembrolizumab) in several different solid tumours (clinicaltrials.gov identifier NCT03625323); a planned Phase I clinical trial referred to as INSIGHT-004 to evaluate a combination of efti with avelumab (clinical trials.gov identifier NCT03252938); and a Phase I combination therapy trial in metastatic melanoma termed TACTI-mel (clinicaltrials.gov identifier NCT02676869).

Further information can be found on the Company's website www.immutep.com or by contacting:

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