Immutep Reports Positive Topline Results from TACTI-003 Phase IIb Trial in First Line Head and Neck Cancer

- Efti in combination with KEYTRUDA® (pembrolizumab) in first line head and neck squamous cell carcinoma (1L HNSCC) led to overall response rates that exceed KEYTRUDA monotherapy across all levels of PD-L1 expression

- In the randomised, controlled Cohort A, the combination shows the strongest performance in patients with high PD-L1 expression (CPS ≥20) with an overall response rate (ORR) of 31.0% as compared to 18.5% for KEYTRUDA monotherapy

- In patients with negative PD-L1 expression (CPS <1, Cohort B), a patient population with no effective chemotherapy-free options, the response rate has substantially improved from the preliminary 26.9% ORR reported in April and topline results with additional data has been accepted for oral presentation at an ESMO Virtual Plenary session on 11th July

- Additional clinical data from TACTI-003 will be presented at a medical conference in H2 CY2024

- Based on the positive topline results, the Company will discuss the path forward in 1L HNSCC with regulatory agencies

- Immutep to host webcast to discuss clinical data today at 9AM AEST (7PM ET, Wednesday 26 June)

SYDNEY, AUSTRALIA – June 27, 2024 – Immutep Limited (ASX: IMM; NASDAQ: IMMP) ("Immutep" or "the Company"), a clinical-stage biotechnology company developing novel LAG-3 immunotherapies for cancer and autoimmune disease, today announces topline results from the TACTI-003 (KEYNOTE-PNC-34) Phase IIb trial evaluating eftilagimod alfa (efti) in combination with MSD's (Merck & Co., Inc., Rahway, NJ, USA) anti-PD-1 therapy KEYTRUDA® (pembrolizumab) as first-line treatment of recurrent/metastatic head and neck squamous cell carcinoma patients (1L HNSCC). The trial enrolled 171 patients with any PD-L1 expression (Combined Positive Score [CPS] ≥1) and negative PD-L1 expression (CPS <1) at over 30 centres across the United States, Europe, and Australia.

Topline Results – overall trial, primary endpoint

Immutep's MHC Class II agonist in combination with KEYTRUDA led to higher overall response rates in evaluable patients according to RECIST 1.1 – the primary endpoint of the study – across all levels of PD-L1 expression (CPS ≥20, CPS 1-19, CPS ≥1, CPS <1) as compared to KEYTRUDA monotherapy (see Table 1). In the overall evaluable TACTI-003 patient population (Cohort A and B), the response rate for efti in combination with KEYTRUDA was ~34% regardless of HPV status and PD-L1 expression, including patients with negative PD-L1 expression.

Dr. Martin Forster of the UCL Cancer Institute and University College London Hospital NHS Foundation, London, UK, and TACTI-003 Investigator, stated, "It is encouraging to see efti safely drive higher response

rates in combination with KEYTRUDA in the first line setting for head and neck squamous cell carcinoma patients, regardless of HPV status and levels of PD-L1. The strong, consistent response rates, irrespective of whether patients have high, low, or negative PD-L1 expression, is intriguing and offers a glimpse into this novel combination's ability to improve patients' clinical responses and expand patient populations that benefit from anti-PD-1 therapy."

Cohort A results – randomised part of trial

In the randomised, controlled Cohort A (N=138; thereof 118 evaluable) comprised of 1L HNSCC patients with any PD-L1 expression (CPS ≥1), the novel immuno-oncology (IO) combination shows the strongest outperformance in patients with high PD-L1 expression (CPS ≥20) with a 31.0% overall response rate (ORR) and 75.9% disease control rate (DCR) in evaluable patients (N=29) as compared to a 18.5% ORR and 59.3% DCR for KEYTRUDA monotherapy in evaluable patients (N=27). High PD-L1 expressing patients represent ~50% of the overall population in 1L HNSCC.

The IO combination also achieved a relatively high ORR of 34.5% in evaluable patients (N=29) with low PD-L1 expression (CPS 1-19). The ORR with KEYTRUDA monotherapy in patients with low PD-L1 expression in TACTI-003 (N=33) was 33.3% and is higher than historical published data for pembrolizumab monotherapy, including a 14.5% ORR in patients with CPS 1-19 in a registrational study[1]. The large difference of the control arm versus historical results in low PD-L1 patients may be explained by imbalances between the TACTI-003 treatment groups, including smoker status and location of primary tumour.

Cohort B results

The Company is also pleased to report that the response rate in patients with negative PD-L1 expression (CPS <1) in Cohort B has substantially improved from the preliminary 26.9% ORR reported in April and that the updated clinical data has been accepted for an ESMO Virtual Plenary session. ESMO Virtual Plenaries are monthly presentations of the latest, original scientific data, including *"Phase II trials which demonstrate remarkable therapeutic benefit, scientific insight or progress in an area of unmet need".* Final topline results including complete response rate in patients with negative PD-L1 expression, who represent ~20% of the overall population in 1L HNSCC, will be delivered via an oral presentation on 11 July 2024. This cohort was not randomised due to ethical reasons as KEYTRUDA monotherapy is not approved for these patients.

Table 1: ORR in Evaluable Patients according to RECIST 1.1

	TACTI-003	
	Efti + KEYTRUDA	KEYTRUDA monotherapy
High PD-L1 Expression (CPS ≥20)	31.0% ORR (N=29)	18.5% ORR (N=27)
Low PD-L1 Expression (CPS 1-19)	34.5% ORR (N=29)	33.3% ORR (N=33)
Any PD-L1 Expression (CPS ≥1)	32.8% ORR (N=58)	26.7% ORR (N=60)
Negative PD-L1 Expression (CPS <1)	26.9% ORR (N=26)[2]	N/A

Safety

With respect to safety, the profile of efti in combination with KEYTRUDA continues to be favourable with no new safety signals as expected.

Dr. Frédéric Triebel, CSO of Immutep, said: "We are pleased with the quality of responses. Once again, durability is tracking well driven by the complementary nature of these two unique immunotherapies in fighting cancer. Efti's distinct activation of dendritic cells as an MHC Class II agonist and the resulting engagement of multiple facets of the adaptive & innate immune system has consistently translated into promising duration of responses in combination with immune checkpoint inhibitors across multiple oncology indications. From a statistical point of view, given the relatively small number of evaluable patients and the very ambitious differences required to generate significance, coupled with unexpected imbalances leading to unanticipated strength in the control arm among patients with low PD-L1 expression, we are excited to see the ~68% differential in the largest patient segment (CPS ≥20) in 1L HNSCC in a randomised setting."

"Additionally, the strength of clinical results in patients with negative PD-L1 expression is notable, and we look forward to sharing more data at the ESMO Virtual Plenary session in July," added Dr. Triebel.

Next Steps

Based on these positive topline results, the Company will discuss potential options with regulatory agencies for metastatic 1L HNSCC patients. More detailed clinical data from TACTI-003 will be presented at a medical conference in H2 CY2024.

Conference Call and Webcast Details

Immutep will host a conference call and webcast to discuss the clinical data. The event will feature CEO Marc Voigt, CSO Dr Frederic Triebel, CMO Dr Florian Vogl, and Christian Mueller, Senior Vice President Strategic Development. An open question & answer session with all presenters will conclude the event. A replay of the webcast will be available under the Events section of Immutep's website.

- Date/Time: Thursday, 27 June, at 9AM AEST (Wednesday, June 26, at 7PM ET)
- Register: Link to register for webcast
- Questions: Investors are invited to submit questions in advance via immutep@morrowsodali.com

Efti has received FDA Fast Track designation in 1L HNSCC regardless of PD-L1 expression.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

About the TACTI-003 Trial

The TACTI-003 (KEYNOTE-PNC-34) trial is an ongoing Phase IIb study evaluating eftilagimod alfa (efti), Immutep's proprietary soluble LAG-3 protein and MHC Class II agonist, in combination with MSD's anti-PD-1 therapy KEYTRUDA® (pembrolizumab) as first line treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC). The randomized Cohort A portion of the study is evaluating efti in combination with pembrolizumab as compared to pembrolizumab monotherapy in patients with PD-L1 positive (Combined Positive Score [CPS] ≥1) tumours, whereas Cohort B is evaluating efti in combination with pembrolizumab in patients with PD-L1 negative tumours.

The primary endpoint of the study is Overall Response Rate of evaluable patients according to RECIST 1.1. Secondary endpoints include Overall Survival, Overall Response Rate according to iRECIST, Progression Free

Survival, and Duration of Response. For more information about the Phase IIb trial, visit clinicaltrials.gov (NCT04811027).

About Eftilagimod Alfa (Efti)
Efti is Immutep's proprietary soluble LAG-3 protein and MHC Class II agonist that stimulates both innate and adaptive immunity for the treatment of cancer. As a first-in-class antigen presenting cell (APC) activator, efti binds to MHC (major histocompatibility complex) Class II molecules on APC leading to activation and proliferation of CD8+ cytotoxic T cells, CD4+ helper T cells, dendritic cells, NK cells, and monocytes. It also upregulates the expression of key biological molecules like IFN-γ and CXCL10 that further boost the immune system's ability to fight cancer.

Efti is under evaluation for a variety of solid tumours including non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC), and metastatic breast cancer. Its favourable safety profile enables various combinations, including with anti-PD-[L]1 immunotherapy and/or chemotherapy. Efti has received Fast Track designation in first line HNSCC and in first line NSCLC from the United States Food and Drug Administration (FDA).

About Immutep
Immutep is a clinical-stage biotechnology company developing novel LAG-3 immunotherapy for cancer and autoimmune disease. We are pioneers in the understanding and advancement of therapeutics related to Lymphocyte Activation Gene-3 (LAG-3), and our diversified product portfolio harnesses its unique ability to stimulate or suppress the immune response. Immutep is dedicated to leveraging its expertise to bring innovative treatment options to patients in need and to maximise value for shareholders. For more information, please visit www.immutep.com.

1. Source: Burtness, B. et al. Pembrolizumab Alone or With Chemotherapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma in KEYNOTE-048: Subgroup Analysis by Programmed Death Ligand-1 Combined Positive Score. Journal of Clinical Oncology 2022 40:21, 2321-2332
2. In patients with negative PD-L1 expression (CPS <1), the 26.9% ORR in evaluable patients from efti in combination with pembrolizumab is the preliminary response rate reported in April 2024. The ORR has improved substantially and will be updated at ESMO Virtual Plenary session in July.

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This announcement was authorised for release by the Board of Immutep Limited.