Press Release
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Immutep reports final positive data in second-line head and neck squamous cell carcinoma at ASCO 2023 Annual Meeting

- **Efti plus pembrolizumab led to deep, durable responses, regardless of PD-L1 expression levels, and median Duration of Response not reached despite median follow up of 39 months in TACTI-002 Phase II**
- **Promising efficacy in patients with a PD-L1 Combined Positive Score (CPS) of greater than or equal to 1 with median Overall Survival of 12.6 months, a 12-month Overall Survival rate of 52.0 percent, and a response rate of 38.5 percent**
- **Patients with a PD-L1 CPS greater than or equal to 20 achieved a median Overall Survival of 15.5 months, a 12-month Overall Survival rate of 66.7 percent, and a response rate of 60.0 percent**
- **One long-lasting complete response occurred in a patient with negative PD-L1 expression or CPS less than 1**
- **Dual immuno-oncology approach is safe and very well tolerated**
- **Follow on TACTI-003 Phase IIb trial in first-line HNSCC expected to report top-line results in H2 of CY2023**

Sydney, Australia, June 5, 2023 – 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 provides an overview of the positive final data from Part C of the TACTI-002 Phase II trial to be presented in a poster presentation at the ASCO 2023 Annual Meeting taking place in Chicago, US.

Part C of TACTI-002 evaluated eftilagimod alpha (efti), a soluble LAG-3 protein and first-in-class MHC Class II agonist, in combination with MSD's (Merck and Co., Inc., Rahway, NJ, USA) anti-PD-1 therapy KEYTRUDA(R) (pembrolizumab) in second-line head and neck squamous cell carcinoma (2L HNSCC) patients unselected for PD- L1 expression (N=37), with disease progression on, or after, platinum-based therapy (± cetuximab).

The combination of efti plus pembrolizumab led to an encouraging overall response rate (ORR) of 29.7 percent and Complete Response (CR) rate of 13.5 percent in 2L HNSCC patients, regardless of PD-L1 expression, as per iRECIST (RECIST 1.1 results were comparable). Responses were seen across all PD-L1 subgroups. A promising ORR of 38.5 percent and 60 percent, median Overall Survival (mOS) of 12.6 and 15.5 months, and 12-month Overall Survival (OS) rate of 52.0 percent and 66.7 percent, were seen in patients with a PD-L1 CPS of greater than or equal to 1 and a PD-L1 CPS greater than or equal to 20, respectively. Despite a long median follow-up of 39 months, median Duration of Response (mDoR) was not reached. (Table 1)

Results compare favourably to reported results from a registrational trial of anti-PD-1 monotherapy in the same patient population with a PD-L1 CPS greater than or equal to 1, which showed a 17.3 percent ORR, mOS of 8.7 months, 12-month OS rate of 40 percent, a CR rate of 2 percent, and mDoR of 18.4 months. *[1]*

Table 1 – Efficacy Endpoints Across PD-L1 Subgroups in second-line HNSCC (TACTI-002, Part C) as per iRECIST

	Overall (N=37)	CPS ≥1 (N=25)	CPS ≥20 (N=15)
Overall Response Rate (ORR),%	29.7	38.5	60.0
Medjan Progression-Free Survival (mPFS), months	2.1	2.3	13.6
6-month PFS rate, %	32.4	40.0	53.3
Median Overall Survival (mOS), months	8.7	12.6	15.5
12-month OS rate,%	46.0	52.0	66.7
Meruan Duration of Response (mDoR), months	Not Reached	Not Reached	Not Reached

Dr. Bernard Doger of START Madrid-FJD, Fundación Jiménez Díaz University Hospital and TACTI-002 and TACTI-003 investigator said, "The high overall and complete response rates for patients in Part C of the TACTI-002 trial, taken alongside their long-lasting persistence with the median Duration of Response not reached, provides a strong foundation for the ongoing TACTI-003 trial in first-line HNSCC. The combination of the MHC Class II agonist, efti, with pembrolizumab is now showing an encouraging overall survival benefit in two different cancer indications."

As seen in multiple clinical trials, efti is generating very durable responses when combined with anti-PD-(L)1 therapies. Notably, one of the five complete responses that lasted 28 months (as of the data cut-off) occurred in a patient with negative PD-L1 expression or CPS less than 1.

The safety profile of efti in combination with pembrolizumab continues to be safe and very well tolerated. No new safety signals were observed from Part C of the TACTI-002 Phase II trial. The dual immuno-oncology approach had adverse reactions that led to treatment discontinuation in only two patients (5.1 percent) *[2]*, which compares favorably to the treatment discontinuation rate from adverse reactions with anti-PD-1 monotherapy in the same patient population (6.1 percent). *[1]*

"It's noteworthy to see efti combined with pembrolizumab generating a response in 29.7 percent of patients with second-line HNSCC, including five patients with complete responses, regardless of PD-L1 expression. In patients expressing PD-L1 CPS greater than 1 or PD-L1 CPS greater than 20, overall survival, progression-free survival, and response rates from the dual immuno-oncology approach compare rather favourably to reported results from anti-PD-1 monotherapy approved for the treatment of platinum-refractory metastatic HNSCC," stated Frédéric Triebel, M.D., Ph.D., Immutep's CSO.

"These final results in second-line HNSCC are very encouraging in a difficult to treat patient population. It was the strength of interim results from TACTI-002, along with efti's potential to address an unmet medical need, that secured FDA Fast Track designation for first-line treatment of HNSCC. In first-line HNSCC, we are now focused on completing enrolment for TACTI-003 by mid-year and expect to report top-line results later in H2 of CY2023," said Marc Voigt, Immutep's CEO.

In addition to the abstract and information that was announced to the ASX on 26 *[3]* and 31 May 2023 *[4]*, the Final results from TACTI-002 Part C: A Phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with metastatic second-line head and neck squamous cell carcinoma unselected for PD-L1 poster will be available on the Posters and Publication section of Immutep's website following its presentation between 2:15PM-5:15PM EDT at ASCO today.

KEYTRUDA(R) is a registered trademark of Merck Sharp and Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ, USA.

[1] Ezra E W Cohen et al., Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study; The Lancet 2019. http://dx.doi.org/10.1016/S0140-6736(18)31999-8
[2] Relationship to efti and/or pembrolizumab could not be ruled out.
[3] Publication of Abstracts for ASCO 2023 Annual Meeting 26 May 2023
[4] Immutep Capital Raising Presentation 31 May 2023 – slides 25 and 26

About Eftilagimod Alpha (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.