Immutep Reports Positive Results in First Line Head and Neck Squamous Cell Carcinoma Patients with Negative PD-L1 Expression

- Efti in combination with KEYTRUDA® (pembrolizumab) achieved a 35.5% response rate in evaluable patients (N=31), according to RECIST 1.1, among the highest recorded for a treatment approach not containing chemotherapy in patients with CPS <1
- High complete response rate of 9.7% with three patients showing a disappearance of cancer lesions post treatment
- Durability of responses tracks well and over 50% of patients received treatment for at least six months
- Combination continues to have a favourable safety profile with no new safety signals observed
- Based on encouraging results and high unmet medical need, the path forward will be discussed with regulatory agencies
- Company to host webcast today at 9am AEST (7pm ET, 11 July), details below

SYDNEY, AUSTRALIA – July 12, 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 positive results from Cohort B of 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 or metastatic head and neck squamous cell carcinoma patients (1L HNSCC) with negative PD-L1 expression. The updated efficacy and safety data was presented by Dr. Robert Metcalf during an oral presentation at the ESMO Virtual Plenary session at 18:30-19:30 CEST on 11 July 2024.

Results

The investigational immuno-oncology (IO) combination utilising efti and KEYTRUDA achieved an objective response rate (ORR) of 35.5% (11 of 31 evaluable patients) and a disease control rate (DCR) of 58.1%, according to RECIST 1.1, in 1L HNSCC patients whose tumours do not express PD-L1 (Combined Positive Score [CPS] <1). These results are among the highest recorded for a chemotherapy-free approach in negative PD-L1 patients and compare favourably to a historical control of 5.4% ORR and 32.4% DCR from anti-PD-1 monotherapy.[1]

Additionally, the IO combination attained a high complete response rate of 9.7% (3 of 31 patients), which compares favourably to a historical control of 0% from anti-PD-1 monotherapy in 1L HNSCC patients with a CPS <1.[2] Notably, one patient with early progressive disease according to RECIST 1.1 has evolved into a confirmed partial responder who remains on therapy after 14 months, resulting in a 38.7% ORR for the IO combination, according to iRECIST.

Robert Metcalf, MD, PhD, The Christie NHS Foundation Trust, Manchester, U.K., stated, "The high response rate from this novel immunotherapy combination is well above other treatment approaches without

chemotherapy. It matches historical response rates from chemotherapy-based treatments but without the associated toxicities. This is really significant for patients with head and neck squamous cell carcinomas who have a CPS less than one and for whom chemotherapy is the current first line treatment. Achieving complete responses in this group bodes well for this immunotherapy combination's future potential, especially given the positive trend in response durability. The clinically meaningful response rate and high unmet medical need warrant further investigation of eftilagimod plus pembrolizumab in this patient population."

Durability of Responses and Favourable Safety

Durability of responses is tracking well as has been seen in other clinical trials when efti is combined with KEYTRUDA. Over 50% of patients in Cohort B received treatment for at least six months with three additional patients nearing this threshold at the time of data cut off (11 March 2024). The combination also continues to have a favourable safety profile with no new safety signals observed.

This new data adds to the body of evidence that efti's novel activation of antigen-presenting cells provides a strong boost to the immune system, enhancing the potential of immune checkpoint inhibitors such as KEYTRUDA. Importantly, as the only MHC Class II agonist in clinical development today, efti is generating a broad anti-cancer immune response in a unique and safe manner across all levels of PD-L1 expression, especially in patients with negative expression (CPS <1).

Next Steps

Based on the encouraging efficacy and high unmet medical need, Immutep will discuss the path forward with regulatory agencies. Efti has received FDA Fast Track designation in 1L HNSCC regardless of PD-L1 expression. The prevalence for CPS <1, CPS 1-19, and CPS ≥20 PD-L1 expression levels are approximately 20%, 30%, and 50% of the HNSCC patient population, respectively.[3]

Webcast Details

Immutep will host a webcast to discuss the clinical data. A replay of the webcast will be available under the Events section of Immutep's website after the event.

Date/Time: Friday, July 12, at 9am AEST (7pm ET July 11)
Register: Link to register for webcast
Questions: Investors are invited to submit questions in advance via immutep@morrowsodali.com

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 (Merck & Co., Inc., Rahway, NJ, USA) 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.

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[1,2] 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. Note, the 5.4% ORR and 32.4% DCR are calculated from the 37 evaluable patients with CPS <1.
[3] Burtness, B. et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study *The Lancet* Volume 394, Issue 10212, P1915-1928, Nov 2019.

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