

Immutep's Efti in Combination with MSD's KEYTRUDA® Leads to Positive Efficacy with Favourable Safety in First Line Head and Neck Cancer

- Results delivered in prestigious Proffered Paper oral presentation at ESMO Congress 2024
- In patients with any PD-L1 expression (CPS ≥ 1), efti in combination with KEYTRUDA outperformance is largest in CPS ≥ 20 with 31.0% ORR (34.5% ORR including partial response after data cut-off) versus 18.5% ORR for KEYTRUDA
- Efti in combination with KEYTRUDA led to a high durability of response of 17.5 months in patients with any PD-L1 expression and combination continues to have favourable safety profile
- Statistically significant increase in absolute lymphocyte count biomarker seen in the efti in combination with KEYTRUDA arm shows efti's biological activity in a randomised setting
- Based on the high unmet need and encouraging results to date, with Overall Survival expected in 2025, the path forward will be discussed with regulatory agencies

SYDNEY, AUSTRALIA – September 16, 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 efficacy and safety results from the TACTI-003 Phase IIb trial evaluating eftilagimod alpha (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).

These results with a data cut-off of 11 March 2024 were selected as a Proffered Paper oral presentation at the European Society for Medical Oncology (ESMO) Congress 2024 and were presented by Claus Kristensen, M.D., Ph.D., Head of Section for Thoracic and Head and Neck Oncology, Rigshospitalet, Copenhagen, Denmark, on 15 September. The data adds to the previously reported overall response rates and safety data on 27 June and 12 July.

Dr. Kristensen stated, "The efficacy and safety data in TACTI-003 are very encouraging and show the significant potential of this novel immunotherapy combination to fight difficult-to-treat head and neck squamous cell carcinomas. The clinically meaningful improvement in responses for patients with high PD-L1 expression in the randomised portion of the trial, combined with the compelling response rates in patients with no PD-L1 expression, are a testament to the complementary nature of efti in combination with KEYTRUDA. I am particularly impressed that these higher response rates and clear increase in biological activity seen in the efti arm do not come at the expense of durability of response or lead to an increased toxicity profile, which is often the case when combining therapies in the search for more efficacious treatments for cancer patients."

Dr. Frédéric Triebel, CSO of Immutep, said "Through multiple clinical trials, we see the promise of efti to not only improve cancer patients' clinical responses to immune checkpoint inhibitors, but also to expand patient populations who respond to them including patients with negative PD-L1 expression. Once again, the TACTI-003 trial has reinforced efti's positive impact on both these fronts. We are excited to see efti in combination

with KEYTRUDA now driving a 1.9-fold increase in responses for head and neck cancer patients with high PD-L1 expression as compared to KEYTRUDA alone, and a statistically significant increase in absolute lymphocyte count in the treatment arm showing efti's biological activity in a randomised setting."

Marc Voigt, CEO of Immutep, added "As we move into the latter half of 2024, we will continue to follow the data in TACTI-003 and start to engage with regulatory authorities regarding potential paths forward. We are certainly pleased with durability we are seeing, which is consistent with other trials in which efti combined with KEYTRUDA achieves a high DOR, unlike many other therapeutic combinations. We are hopeful this positive duration of response continues and, as seen in first line non-small cell lung cancer in the TACTI-002 trial evaluating efti in combination with KEYTRUDA, eventually contributes to an overall survival benefit for patients with first line head and neck cancer."

ESMO Congress 2024 Proffered Paper Oral Presentation

Title: Primary Results from TACTI-003: A Randomized Phase IIb Trial Comparing Eftilagimod Alpha (soluble LAG-3) Plus Pembrolizumab Versus Pembrolizumab Alone in First-Line Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma with CPS ≥ 1

Clinical Highlights from Randomised Cohort A in 1L HNSCC Patients with Any PD-L1 Expression (CPS ≥ 1)

Efti leads to higher Objective Response Rates (ORR)

- Efti in combination with pembrolizumab (E+P) led to a 32.8% ORR (34.5% including one partial response reported after data cut-off) in evaluable patients with CPS ≥ 1 (N=58) compared to 26.7% for pembrolizumab in evaluable patients with CPS ≥ 1 (N=60), according to RECIST 1.1. Imbalances of prognostic markers towards the pembrolizumab alone arm included HPV status, smoking status, and primary tumour location.
- E+P outperformance in patients with any PD-L1 expression was strongest in high PD-L1 expressing patients (CPS ≥ 20) with a 31.0% ORR (N=29) versus an 18.5% ORR for pembrolizumab alone (N=27), along with a complete response rate of 6.9% in E+P arm versus 3.7% for pembrolizumab alone. An additional partial response was reported in CPS ≥ 20 after data cut-off leading to a 34.5% ORR, a 1.9-fold increase in responses over pembrolizumab alone in this patient group.

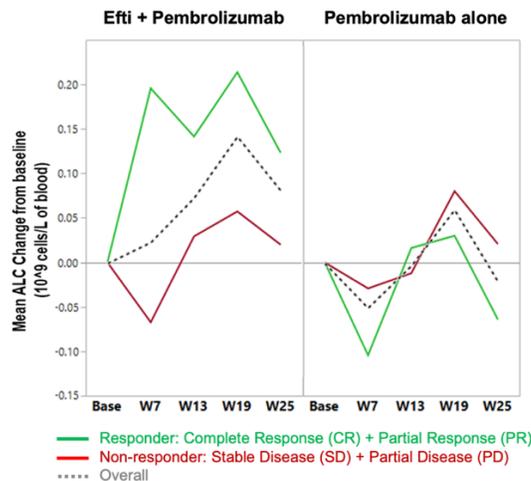
Efti maintains a high Duration of Response (DOR)

- Durability of response was achieved with the addition of efti with a median DOR of 17.5 months in the E+P arm (N=58) as compared to 17.1 months in the pembrolizumab alone arm (N=60)
 - Data compares favourably to other anti-PD-1 combinations with cytotoxic drugs like chemotherapy or EGFR inhibitors, including a historical DOR of ~6 to ~7 months from anti-PD-1 combined with chemotherapy in 1L HNSCC¹⁻⁴

Efti increases Biological Activity

- A statistically significant increase in absolute lymphocyte count (ALC), measured as an exploratory biomarker, was seen in the E+P arm as shown in the graphic below, indicating an effective efti-induced immune response in this randomised setting

- o ALC increase is in line with data from other Phase II trials evaluating efti in combination with chemotherapy in metastatic breast cancer or pembrolizumab in non-small cell lung cancer⁵⁻⁶



Efti continues to have favourable safety profile

- Efti in combination with pembrolizumab continues to have a favourable safety profile with no new safety signals observed
 - o Discontinuation rate from treatment emergent adverse events was similar for both E+P (4.3%) and for pembrolizumab alone (4.4%)
 - o Unlike other combinations with anti-PD-1 therapy, E+P continues to have a comparable safety profile to pembrolizumab alone other than injection site reactions as expected with efti’s subcutaneous delivery

Additionally, E+P drives a high ORR and Disease Control Rate (DCR) in 1L HNSCC patients regardless of PD-L1 expression. In Cohorts A and B together (N=89), E+P achieved a 33.7% ORR (34.8% including one partial response reported after data cut-off) including 31 patients in Cohort B with negative PD-L1 (CPS <1). E+P also achieved a higher DCR compared to pembrolizumab monotherapy across all PD-L1 expression levels, with a consistent increase from 58.1% DCR in CPS <1, to 69.0% DCR in CPS 1-19, to 75.9% DCR in CPS ≥20.

This new data adds to the body of evidence that efti’s activation of antigen-presenting cells provides a strong boost to the immune system, enhancing the potential of immune checkpoint inhibitors (ICI) such as KEYTRUDA. As the only MHC Class II agonist in clinical development today, efti generates a broad anti-cancer immune response in combination with ICIs regardless of PD-L1 expression, including for patients with negative PD-L1 expression, in a unique and safe manner across multiple different cancers.

The ESMO Preferred Paper Oral Presentation slides are available on the [Posters & Publications](#) section of ImmuteP’s website.

Next Steps

ImmuteP will continue to follow the maturing data from TACTI-003, with the most relevant endpoint of Overall Survival expected in 2025, and engage with regulatory authorities regarding potential paths forward.

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

About TACTI-003

The Two ACTIVE Immunotherapies-003 (TACTI-003) trial is an ongoing Phase IIb study (also known as KEYNOTE-C34) evaluating eftilagimod alpha (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 (CPS <1).

The primary endpoint of the study is Objective Response Rate of evaluable patients according to RECIST 1.1. Secondary endpoints include Overall Survival, Objective Response Rate according to iRECIST, Progression Free Survival, and Duration of Response. For more information about the Phase IIb trial, visit [clinicaltrials.gov \(NCT04811027\)](https://clinicaltrials.gov/NCT04811027).

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