Immutep's Efti Shows Excellent Survival Data from INSIGHT-003 Trial in Non-Small Cell Lung Cancer

- Mature data in patients with a minimum follow-up of 22 months (N=21) shows excellent results, well above historical controls and exceeding expectations:
  - Median Overall Survival is 32.9 months, with median Progression Free Survival reaching 12.7 months, and a 24-month Overall Survival rate of 81.0%
- Data from all evaluable patients to date (N=40) demonstrates significant improvement of Overall Response Rate compared to historical controls
- Safety continues to be favourable with no new safety signals
- INSIGHT-003, which is nearing completion of enrolment, evaluates efti with the most widely used immunotherapy-chemo combination today in a similar population to upcoming TACTI-004 Phase III trial

SYDNEY, AUSTRALIA – November 14, 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 data from the investigator-initiated INSIGHT-003 Phase I trial evaluating eftilagimod alpha (efti) in combination with KEYTRUDA® (pembrolizumab) and chemotherapy for first-line treatment of metastatic non-squamous non-small cell lung cancer (1L NSCLC) patients.

Prof. Dr. Salah-Eddin Al-Batran of the Frankfurt Institute of Clinical Cancer Research (IKF) and project lead stated, "The strength of these mature survival results coupled with a favourable safety profile in first-line treatment of patients with non-squamous NSCLC, the vast majority of whom have negative or low PD-L1 expression, is very encouraging. This promising data in INSIGHT-003 suggests a complementary effect from the addition of efti, a unique MHC Class II agonist, to the standard-of-care combination of pembrolizumab and chemotherapy which has revolutionised the treatment landscape in lung cancer. The IKF will also support and is looking forward to participating in the upcoming TACTI-004 study, which has PFS and OS as dual primary endpoints."

Key Results - Data cutoff - 15 October 2024

The survival data from the triple combination therapy in patients irrespective of PD-L1 expression with a minimum follow-up of 22 months (N=21) at data cut-off shows:

INSIGHT-003 Results	
Median Overall Survival (OS)	32.9 months
Median Progression-Free Survival (PFS)	12.7 months
24-month Overall Survival (OS)	81.0%

These results compare favourably to the 22.0-month median OS, 9.0-month median PFS, and 24-month OS rate of 45.5% from a registrational trial of anti-PD-1 and doublet chemotherapy in non-squamous 1L NSCLC regardless of PD-L1 expression.[1] Notably, ~19% of the 21 patients in INSIGHT-003 with mature survival data have high PD-L1 expression, who typically respond better to anti-PD-1 therapy, versus ~32% in the registrational trial of anti-PD-1 and doublet chemotherapy.

Marc Voigt, CEO of Immutep, stated, "The overall survival and progression-free survival data from this mature cohort of patients in INSIGHT-003 with nearly a 2-year minimum follow-up exceeds our expectations. We are encouraged to see efti build upon the historical clinical outcomes from the most widely used immunotherapy-chemo combination today. Additionally, the early evaluations in the expansion cohort of 19 patients, who all have low or negative PD-L1 expression, are tracking well and we look forward to additional data updates from the INSIGHT-003 trial in 2025 and beyond. Our focus on potentially driving a new standard of care globally in first line treatment of NSCLC is boosted by these results and we are well advanced in our preparations to initiate the TACTI-004 Phase III trial."

Data from all evaluable patients to date (N=40) demonstrates significant improvement of Overall Response Rate (ORR) according to RECIST 1.1 across all levels of PD-L1 expression compared to historical control[2]:

- 75.0% ORR versus 62.1% ORR in patients with high PD-L1 expression (TPS >50%)
- 58.8% ORR versus 49.2% ORR in patients with low PD-L1 expression (TPS 1-49%)
- 47.4% ORR versus 32.3% ORR in patients with negative PD-L1 expression (TPS <1%)

In this all-comer PD-L1 trial, the 55.0% ORR and 87.5% Disease Control Rate (DCR) are from the following breakdown of patients by PD-L1 expression: TPS ≥50% (N=4), TPS 1-49% (N=17), and TPS <1% (N=19). As compared to the general 1L NSCLC patient population of which each of these PD-L1 levels represents roughly one-third, INSIGHT-003 is biased towards low and negative PD-L1 (TPS <50%) patients who are typically less responsive to anti-PD-1 therapy.

In these patients with low and negative PD-L1 expression (36 of 40 patients), the triple combination achieved a 52.8% ORR and 86.1% DCR. Of note, all 19 patients in the expansion cohort have TPS <50% and several with stable disease have potential to become responders.

Safety

Safety continues to be favourable for efti in combination with pembrolizumab and chemotherapy, with no new safety signals.

Next Steps

INSIGHT-003, a multi-centre study led by the Frankfurt Institute of Clinical Cancer Research IKF, is nearing completion of patient enrolment. Additional data updates from this trial are expected in 2025 and beyond.

About INSIGHT-003

INSIGHT-003 is an investigator-initiated, multi-centre study led by the Frankfurt Institute of Clinical Cancer Research (IKF). It is being run as the third arm (Stratum C) of the ongoing Phase I INSIGHT trial with Prof. Dr. Salah-Eddin Al-Batran as lead investigator. The study is evaluating a triple combination therapy in front line non-small cell lung cancer patients consisting of efti administered subcutaneously in conjunction with an existing approved standard-of-care combination of anti-PD-1 therapy (pembrolizumab) and doublet chemotherapy (carboplatin and pemetrexed) delivered intravenously. The trial will assess the safety, tolerability, and initial efficacy of the combination.

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. Shirish Gadgeel et al., Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non–Small-Cell Lung Cancer. JCO 38, 1505-1517(2020). DOI:10.1200/JCO.19.03136

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