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Immutep announces promising new clinical data from triple combination therapy in INSIGHT-003 trial

- **Efti plus standard-of-care anti-PD-1 therapy and doublet chemotherapy in first-line non-small cell lung cancer is well tolerated and continues to show promising initial signals of efficacy**
- **Triple combination therapy has achieved a 67 percent response rate and 91 percent disease control rate in metastatic first-line non-small cell lung cancer patients (N=21) despite 81 percent of patients having low or negative PD-L1 expression**

Sydney, Australia, May 24, 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 announces new encouraging clinical data in first-line non-small cell lung cancer from INSIGHT-003, an investigator-initiated Phase I trial conducted by the Frankfurt Institute of Clinical Cancer Research IKF. INSIGHT-003 is the first study evaluating eftilagimod alpha ("efti"), a soluble LAG-3 protein and MHC Class II agonist, in conjunction with standard-of-care anti-PD-1 therapy and doublet chemotherapy (carboplatin/pemetrexed).

The triple combination therapy remains well-tolerated and continues to show promising initial efficacy signals attaining a 67 percent overall response rate (ORR) and 91 percent disease control rate (DCR) in advanced or metastatic non-squamous first-line non-small cell lung cancer patients (N=21). Notably, 81 percent (17/21) of patients had a PD- L1 Tumor Proportion Score (TPS) of less than 50 percent, who are less responsive to anti-PD-1 based therapy compared with PD-L1 high expressing patients.

The 67 percent ORR regardless of PD-L1 expression and 65 percent response rate in patients with PD-L1 TPS less than 50 percent for the triple combination compare favourably to reported results from a registrational trial of anti-PD-1 and doublet chemotherapy in the same patient population that yielded an ORR of 48 percent regardless of PD-L1 expression and a response rate of 40.8 percent in patients with PD-L1 TPS less than 50 percent.

Immutep CSO, Dr. Frédéric Triebel, said: "Immutep has made significant progress with our late-stage development planning to treat one of the largest cancer indications globally. We are uniquely positioned to address PD-L1 low (TPS 1-49 percent) and high (TPS greater than 50 percent) expressing patients, representing roughly 65 percent of the non-small cell lung cancer patient population, with powerful chemo-free IO-IO approaches, and potentially the entire patient population when including the IO-IO-chemo combination being tested in INSIGHT-003. Powering both options is eftilagimod alpha, the only MHC Class II agonist in clinical development, safely generating a broad immune response to fight cancer."

Patients with high, low, and negative PD-L1 expression represent approximately 30 percent, 35 percent, and 35 percent, respectively, of the first-line non-small cell lung cancer (1L NSCLC) patient population. Low and negative PD-L1 expressors (patients with a PD-L1 TPS of 1-49 percent and less than 1 percent) are less responsive to anti-PD-(L)1 therapy compared to patients with high levels or PD-L1 TPS of greater than or equal to 50 percent.

Unlike many immuno-oncology combinations (IO-IO) that focus on high PD-L1 expressing patients, compelling clinical results to date from the TACTI-002 Phase II trial suggest that efti may be uniquely positioned to effectively address low and high PD-L1 expressors (approximately 65 percent of 1L NSCLC patient population) through chemo-free IO-IO combinations, and potentially the entire NSCLC patient population, regardless of PD-L1 expression, when adding the IO-IO-chemo triple combination.

Prof. Dr. Salah-Eddin Al-Batran of the Institute of Clinical Cancer Research IKF and lead investigator noted: "These initial results are supportive of efti's synergies with both anti-PD-1 therapy and chemotherapy in the clinical setting, and we are pleased with the data to date from this novel IO-IO-chemo combination. Efti's ability to safely engage such a robust immune response for cancer patients via MHC Class II agonism is truly unique, and we look forward to providing more data from this triple combination therapy at a major medical conference this year."

The INSIGHT-003 trial was recently expanded to enroll 50 patients across multiple sites based on the favourable safety and efficacy results, and additional data is expected to be presented at a major medical conference in H2 CY2023.

About INSIGHT-003
INSIGHT-003 is an investigator-initiated study conducted by the 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 chemotherapy (carboplatin and pemetrexed) delivered intravenously. The trial will assess the safety, tolerability, and initial efficacy of the combination.

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.