ASX/Media Release

Immutep Announces Initiation of Phase II/III Trial for Eftilagimod Alpha plus Paclitaxel in Metastatic Breast Cancer

- Integrated Phase II/III trial design incorporates feedback from the FDA and EMA and will help inform a BLA and MAA
- HR+/HER2-neg/low metastatic breast cancer (MBC) patient population has been expanded to include triple-negative breast cancer, which together account for ~78% of breast cancer cases
- Approval for study start received in US and IRB approval in Spain, with more countries to follow shortly
- First patient expected to be enrolled in early Q2 CY2023
- As a first-in-class APC activator, efti is well positioned to enhance standard-of-care chemotherapy in MBC

SYDNEY, AUSTRALIA – 14 March 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 announced the initiation of AIPAC-003 (**A**ctive **I**mmunotherapy, Eftilagimod Alpha, and **PAC**litaxel), an integrated Phase II/III trial to evaluate eftilagimod alpha ("efti") in combination with paclitaxel for the treatment of metastatic HER2-neg/low breast cancer (MBC). Regulatory approval has been received in the US and Institutional Review Board (IRB) approval has been received in Spain, with approvals in additional countries anticipated to follow shortly. The first patient is expected to be enrolled in early Q2 CY2023.

As a first-in-class soluble LAG-3 protein targeting MHC Class II ligands on antigen-presenting cells (APC), efti is uniquely positioned to improve clinical outcomes from standard-of-care chemotherapy. Its activation of APCs (e.g., dendritic cells, monocytes) triggers a broad immune response that includes significant increases in cytotoxic CD8+ T cells armed with chemo-induced tumour antigens to target cancer. This synergy was demonstrated by the AIPAC Phase IIb trial's encouraging efficacy and safety, including a +2.9-month median overall survival (mOS) improvement, statistically significant mOS improvements between 4.2 to 19.6 months across three pre-specified subgroups, a statistically significant increase in cytotoxic CD8 T cells that correlated with improved OS, a higher 48% ORR (vs 38% for chemo alone), and a superior Quality of Life preservation.

Immutep CEO, Marc Voigt, said: "With its novel mechanism of action to activate antigen-presenting cells, efti has to date safely improved clinical outcomes from anti-PD-(L)1 therapies and standard-of-care chemotherapy. We look forward to AIPAC-003 building upon the encouraging synergy seen in our previous Phase IIb trial in metastatic breast cancer, especially with its three key adaptations: same day administration of efti plus paclitaxel, this dual IO-chemotherapy treatment continuing until disease progression, and a new primary endpoint of overall survival. The selected Phase II/III trial design allows us to move forward with a risk-balanced approach in MBC, as we continue our prioritized late-stage clinical development with anti-PD-1 therapy in 1st line head & neck squamous cell carcinoma and 1st line non-small cell lung cancer."

The Company and the US Food and Drug Administration (FDA) agreed to the integrated Phase II/III trial design for AIPAC-003 that will help inform a Biologics License Application (BLA). Additionally, the trial design

incorporates feedback from Scientific Advice meetings with the European Medicines Agency (EMA) to support a Marketing Authorisation Application (MAA).

Based on feedback from the FDA/EMA, the HR+/HER2-neg/low MBC patient population has been expanded to include triple-negative breast cancer (TNBC), an aggressive cancer with limited treatment options, which together account for ~78% of breast cancer cases. The Company and the FDA also agreed to an open-label lead-in component of 6 to 12 patients to test 90mg efti dosing in combination with paclitaxel driven by efti's excellent safety profile, along with the FDA's Project Optimus initiative in oncology. Additionally, patients will receive same-day administration of efti + paclitaxel that can continue until disease progression, unlike the prior AIPAC trial that administered both on different days and stopped chemotherapy at six months.

The open-label lead-in of up to 12 patients will be followed by a randomized (1:1) portion of the Phase II consisting of up to 58 patients that will receive 30mg efti or 90mg efti to determine the optimal biological dose in combination with paclitaxel. Depending on the Phase II results, potential regulatory actions and resources, a randomized, double-blinded, placebo-controlled Phase III portion will then follow. The Phase III will have overall survival as the primary objective and may include a specific patient population.

With respect to the late-stage clinical development of efti, the Phase II portion of the MBC trial, the ongoing randomized/controlled Phase II trial in 1st line HNSCC, and the initiation of the registrational trial in 1st line NSCLC are included in the budget and have no impact on the Company's expected cash runway to the end of the 1st half of calendar year 2024.

About Eftilagimod Alpha (Efti)
Efti is Immutep's proprietary soluble LAG-3 clinical stage candidate that is a first-in-class antigen-presenting cell (APC) activator that stimulates both innate and adaptive immunity for the treatment of cancer. Efti binds to and activates antigen presenting cells via MHC II molecules leading to expansion 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 HER2–/HR+ 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 1st line HNSCC and in 1st 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.

Australian Investors/Media:
Catherine Strong, Citadel-MAGNUS
+61 (0)406 759 268; cstrong@citadelmagnus.com

U.S. Media:
Chris Basta, VP, Investor Relations and Corporate Communications
+1 (631) 318 4000; chris.basta@immutep.com

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