Immutep Announces Initial Safety Data from First-in-Human Phase I Trial Evaluating IMP761

- Favourable safety profile for world's first LAG-3 agonist, IMP761, with no treatment related adverse events to date
- Additional safety data and assessment of PK/PD relationships to follow in first half of CY2025
- IMP761 is designed to enhance the "brake" function of LAG-3 on T cells to restore balance to the immune system and address the underlying cause of many autoimmune diseases

SYDNEY, AUSTRALIA – 17 December 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 favourable initial safety data from the placebo-controlled, double-blind first-in-human Phase I study evaluating IMP761. Through the first three of five single ascending dose cohorts in healthy participants, there have been no treatment related adverse events.

Dr. Frédéric Triebel, CSO of Immutep, said: "We are very encouraged by the safety data generated to date for IMP761, the world's first LAG-3 agonist antibody, in this Phase I setting. Derisking this promising asset in this proof-of-concept study in healthy subjects assessing its safety and immunosuppressive efficacy on an antigen-specific T-cell mediated intra-dermal reaction is an important step for this exciting program in autoimmune diseases. Given that IMP761 is potentially addressing the root cause of many different autoimmune diseases, we are eager to see this study generating more data."

The trial in up to 49 participants is being conducted by the Centre for Human Drug Research (CHDR) in Leiden, the Netherlands. In addition to the safety analysis, CHDR is implementing its keyhole limpet haemocyanin (KLH) challenge model to evaluate IMP761's pharmacological activity. Additional safety data and assessment of pharmacokinetic/pharmacodynamic (PK/PD) relationships to follow in the first half of CY2025.

The LAG-3 (lymphocyte-activation gene-3) immune checkpoint has been identified as a promising target for an agonist antibody to treat rheumatoid arthritis, Type 1 diabetes, and multiple sclerosis, among potentially many other autoimmune diseases.[1,2,3] This first-in-class agonist LAG-3 antibody is designed to restore balance to the immune system by enhancing the "brake" function of LAG-3 to silence dysregulated self-antigen-specific memory T cells that cause many autoimmune diseases. In preclinical studies, IMP761 has led to a large decrease in inflammatory cytokines and demonstrated its effectiveness in suppressing antigen-specific T cell–mediated immune responses.[4,5]

For more information on the trial, please visit clinicaltrials.gov (NCT06637865).

About IMP761

IMP761, a first-in-class immunosuppressive lymphocyte-activation gene-3 (LAG-3) agonist antibody, has the potential to address the root cause of many autoimmune diseases by specifically silencing autoimmune memory T cells that accumulate at disease sites and restoring balance to the immune system. As published in the Journal of Immunology, encouraging pre-clinical *in vivo* and *in vitro* studies show IMP761 inhibits peptide-

induced T cell proliferation, activation of human primary T cells, and an antigen-specific delayed-type hypersensitivity (DTH) reaction. Additional preclinical data in oligoarticular juvenile idiopathic arthritis (o-JIA) published in Pediatric Research details how IMP761 led to a decrease in a broad spectrum of effector cytokines in just 48 hours. This study also showed children with o-JIA have a skewed LAG-3 metabolism and suggested they can benefit from agonistic LAG-3 activity.

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.

1. Pedersen, J.M., Hansen, A.S., Skejø, C. et al. Lymphocyte activation gene 3 is increased and affects cytokine production in rheumatoid arthritis. Arthritis Res Ther 25, 97 (2023). https://doi.org/10.1186/s13075-023-03073-z

2. Jones BE, Maerz MD et al. Fewer LAG-3+ T Cells in Relapsing-Remitting Multiple Sclerosis and Type 1 Diabetes. J Immunol. 2022 Feb 1;208(3):594-602. doi: 10.4049/jimmunol.2100850. Epub 2022 Jan 12. PMID: 35022272; PMCID: PMC8820445.

3. Zhou X, Gu Y et al. From bench to bedside: targeting lymphocyte activation gene 3 as a therapeutic strategy for autoimmune diseases. Inflamm Res. 2023 Jun;72(6):1215-1235. doi: 10.1007/s00011-023-01742-y. Epub 2023 Jun 14. PMID: 37314518.

4. Mathieu Angin, Chrystelle Brignone, Frédéric Triebel; A LAG-3–Specific Agonist Antibody for the Treatment of T Cell–Induced Autoimmune Diseases. J Immunol 15 February 2020; 204 (4): 810–818. https://doi.org/10.4049/jimmunol.1900823

5. Sag, E., Demir, S., Aspari, M. et al. Juvenile idiopathic arthritis: lymphocyte activation gene-3 is a central immune receptor in children with oligoarticular subtypes. Pediatr Res 90, 744–751 (2021). https://doi.org/10.1038/s41390-021-01588-2

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