ASX/Media Release

Immutep Receives Regulatory Clearance for Phase I Study of First-in-Class LAG-3 Agonist Antibody Designed to Treat Autoimmune Diseases

- Study expected to enrol first participants during Q3 CY2024

SYDNEY, AUSTRALIA – 17 July 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 it has received regulatory clearance from the ethics and competent authority in the Netherlands to initiate the first-in-human Phase I study of IMP761.

IMP761 is the world's first therapeutic LAG-3 agonist antibody and as such is uniquely positioned in the treatment landscape for autoimmune diseases. The immune checkpoint LAG-3 has been identified as a promising target for agonist immunotherapy to treat rheumatoid arthritis, Type 1 diabetes, and multiple sclerosis, among other autoimmune diseases.[1,2,3] IMP761 is designed to restore balance to the immune system by enhancing the "brake" function of LAG-3 to silence unregulated self-antigen-specific memory T cells. These T cells accumulate at disease sites and are the underlying cause of many autoimmune diseases.

Professor Bent Deleuran, MD, Department of Biomedicine, Aarhus University (DK) stated, "Immune checkpoint molecules such as LAG-3 play pivotal roles in determining the outcome of antigen activation, and as a result hold significant potential in the treatment of autoimmune diseases. In preclinical studies, the agonistic LAG-3 antibody IMP761 has shown, both in vitro and in vivo, to be highly effective in suppressing antigen-specific T cell–mediated immune responses and driving a meaningful decrease in inflammatory cytokines. It is exciting to see IMP761 move into the clinical setting to evaluate the potential of this new immunotherapy to address autoimmune diseases."

"The regulatory and ethical clearance for the first-in-human trial of IMP761 is a significant milestone for Immutep and marks an important step in the development of this novel autoimmune disease approach," said Dr. Frédéric Triebel, Immutep's CSO. "Blocking LAG-3 with an antagonist antibody in cancer patients unleashes the power of the anti-tumor T cell responses, but also leads to autoimmunity in a fraction of the patients. This has put LAG-3 at the center of autoimmune disorders as a co-inhibitory receptor that downplays the T cell receptor response. Using IMP761, an agonist LAG-3 antibody, to reinforce this physiological upstream control of the T cell response represents a new approach to silence the few aggressive T cells that lead to autoimmune diseases," added Dr. Triebel.

The single and multiple ascending dose, placebo-controlled, double-blind, Phase I study is being conducted by the Centre for Human Drug Research (CHDR), a world-class institute in Leiden, the Netherlands specializing in cutting-edge early-stage clinical drug research. The study aims to enrol 49 healthy volunteers, with the objective of assessing safety, pharmacokinetics (PK) and pharmacodynamics (PD). CHDR will implement its unique keyhole limpet haemocyanin (KLH) challenge model allowing for the evaluation of IMP761's pharmacological activity at the earliest stages of clinical development.

Immutep anticipates that CHDR will enrol first participants into the Phase I study during Q3 of CY2024 with first data being available before end of the year.

About IMP761

IMP761, a first-in-class immunosuppressive 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.

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