ASX/Media Release

Immutep Reports New Positive Interim Data from its Phase II Study of LAG-3 Candidate, Eftilagimod Alpha, in 2nd line PD-X refractory NSCLC

- Encouraging efficacy results continue for patients with 2nd line PD-X refractory non-small cell lung cancer (NSCLC)
- Patients in this 2nd line setting had confirmed disease progression on anti-PD-1 / anti-PD-L1 ("PD-X") based 1st line therapy[1]
- Key facts reported:
  - Median Overall Survival (OS) from therapy with efti in combination with pembrolizumab is 9.7 months
  - 25% were progression free at 6 months and 36.5% were alive at 18 months[2]
- Chemo-free therapy of efti in combination with pembrolizumab continues to be safe and well tolerated, comparing favourably to standard of care chemotherapy-based options

SYDNEY, AUSTRALIA – 1 August 2022 – Immutep Limited (ASX: IMM; NASDAQ: IMMP) ("Immutep" or "the Company"), a biotechnology company developing novel LAG-3-related immunotherapy treatments for cancer and autoimmune disease, is pleased to announce new interim data from 2nd line NSCLC patients (Part B) in the Phase II TACTI-002 trial. The data was presented as part of the electronic poster presentation at the IASLC 2022 World Conference on Lung Cancer (WCLC 2022) being held in Vienna, Austria and is also available on the Company's website.

This part of TACTI-002 (Part B), evaluates Immutep's lead product candidate, eftilagimod alpha ("efti" or "IMP321") in combination with MSD's KEYTRUDA® (pembrolizumab) in a total of 36 patients with 2nd line PD-X refractory metastatic NSCLC who were not pre-selected for their PD-L1 status. The data cut-off date is 1 July 2022.

In this 2nd line setting, patients were treated with pembrolizumab, which is an anti-PD-1 therapy, in combination with efti despite having confirmed disease progression on PD-X based therapy in the 1st line setting.[3] This was to evaluate whether efti with its unique mechanism of action in combination with pembrolizumab might provide a benefit for these patients that would otherwise move on to chemotherapy in 2nd line. Typically this standard of care 2nd line chemotherapy would be just single agent taxane chemotherapy, as the majority of patients received platinum based doublet chemotherapy plus PD-X therapy in the 1st line setting.

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[1] Disease progression was confirmed by two consecutive CT-scans at least four weeks apart, eliminating the possibility of pseudo-progressions.

[2] Calculated by Kaplan-Meier estimates

[3] Excluding any so called "pseudo-progressors". A pseudo-progression refers to an increase in the apparent size of a tumour or number of metastases on an imaging test, that can falsely create the appearance of disease progression. This may be caused by the infiltration of immune cells into the tumour site or a delay in the development of an adaptive immune response following immunotherapy.

Thus, the enrolled patients were advanced in their disease with limited treatment options.

Immutep CSO and CMO, Dr Frederic Triebel, said: "It is encouraging to see efti in combination with pembrolizumab continues to report promising antitumour and safety results in 2nd line NSCLC. In particular, efti in combination with pembrolizumab is demonstrating sustained survival compared with standard of care chemotherapy regimens, and favourable safety and tolerability. Of course, for patients with such advanced disease, having a chemo-free alternative could mean a very real difference to their quality of life."

"Furthermore, these results provide promising insights into how efti may provide a meaningful patient benefit in other PD-X refractory indications in the future," he said.

TACTI-002 Investigator, Dr Martin Forster of the UCL Cancer Institute and University College London Hospital NHS Foundation, London, UK, said: "The TACTI-002 trial is showing 36.5% of patients have survived for at least 18 months when receiving efti in combination with pembrolizumab. The median overall survival is 9.7 months which is a meaningful survival benefit, plus disease control and durability have also continued favourably as the trial has advanced. All these results support further clinical investigation of efti in combination with pembrolizumab in PD-X resistant NSCLC patients."

Condition of Patients

All enrolled patients had confirmed progressive disease on or after standard of care 1st line therapy with PD-X monotherapy (33%) or a combination of PD-X therapy and platinum-based doublet chemotherapy (67%). These patients are therefore resistant to PD-X based therapy and are referred to as "PD-X refractory". Per standard clinical practice, they would otherwise usually go on to single agent chemotherapy if they received combination PD-X therapy and platinum based doublet chemotherapy in 1st line or, alternatively, go on to doublet chemotherapy if they received PD-X monotherapy in 1st line. A vast majority (75%) of enrolled patients had a PD-L1 tumour proportion score (TPS) of < 50%.

Accordingly, the enrolled patients represent a challenging to treat patient population with limited current treatment options.

Key Findings – data cut-off 1 July 2022

- Median OS of 9.7 months for those who received chemo-free therapy of efti in combination with pembrolizumab, which is comparable with current standard of care chemotherapy options in this 2nd line setting[4]
- Favourable sustained survival with 36.5% of patients alive at 18 months[5]
- 36.1% (13/36) Disease Control Rate (DCR) and disease control (progression free) in 25% of patients at 6 months
- Durable responses of 10+ months in 5.6% (2/36) of patients, with both patients continuing in the trial for over 11 months and 24+ months

[4] Docetaxel and pemetrexed are approved by the FDA for treatment of 2nd line NSCLC:
See Shepherd et al *J Clin Oncol* 2000 May18(10):2095-103 and Hanna et al *J Clin Oncol* 2004 May 1;22(9):1589-97 which reported a median patient survival of 7 months and 8.3 months from treatment with docetaxel and pemetrexed, respectively, in 2nd line NSCLC.
[5] Compared to 15-25% with standard of care docetaxel chemotherapy (source CM-017; CM-057).

Table 1 – TACTI-002 Interim Results for Part B of TACTI-002

Tumour Response	Part B 2nd line NSCLC[6]
Response as per iRECIST	**Stage 1 & 2 N (%) Total N=36**
Complete Response (CR)	0 (0)
Partial Response (PR)	2 (5.6)
Stable Disease (SD)	11 (30.6)
Progressive Disease (PD)	22 (61.1)
Not Evaluable	1 (2.8)
Overall Response Rate (ITT)	**2/36 (5.6)**
Disease Control Rate (ITT)	**13/36 (36.1)**
Overall Response Rate (evaluable patients)	**2/35 (5.7)**
Disease Control Rate (evaluable patients)	**13/35 (37.1)**

Safety
Efti in combination with pembrolizumab continues to be safe and well-tolerated, with no new safety signals. Efti's good safety profile to date compares favourably to standard of care chemotherapy options.

Conclusion
Efti in combination with pembrolizumab is continuing to demonstrate encouraging early signs of antitumour activity in 2nd line confirmed PD-X refractory, NSCLC patients.

About the TACTI-002 Trial
TACTI-002 (Two ACTive Immunotherapies) is being conducted in collaboration with Merck & Co., Inc., Rahway, NJ, USA (known as "MSD" outside the United States and Canada). The study is evaluating the combination of eftilagimod alpha (efti) with MSD's KEYTRUDA® (pembrolizumab) in patients with second line head and neck squamous cell carcinoma or non-small cell lung cancer in first and second line.

The trial is a Phase II, Simon's two-stage, non-comparative, open-label, single-arm, multicentre clinical study that is taking place in study centres across Australia, Europe, and the US.

Patients participate in one of the following:

- Part A - first line non-small cell lung cancer (NSCLC), PD-X naïve - given the promising results of the first two stages of Part A, an expansion stage with 74 additional patients was commenced in November 2020 to assist with trial design in subsequent late-stage settings
- Part B - second line NSCLC, PD-X refractory

[6] As assessed by local investigator read.

- Part C - second line head and neck squamous cell carcinoma (HNSCC), PD-X naïve

TACTI-002 is an all-comer study in terms of PD-L1 status, a well-known predictive marker for response to pembrolizumab monotherapy especially in NSCLC and HNSCC.

More information about the trial can be found on Immutep's website or on ClinicalTrials.gov (Identifier: NCT03625323).

About Immutep
Immutep is a globally active biotechnology company that is a leader in the development of LAG-3 related immunotherapeutic products for the treatment of cancer and autoimmune disease. Immutep is dedicated to leveraging its technology and expertise to bring innovative treatment options to market for patients and to maximize value to shareholders. Immutep is listed on the Australian Securities Exchange (IMM), and on the NASDAQ (IMMP) in the United States.

Immutep's current lead product candidate is eftilagimod alpha ("efti" or "IMP321"), a soluble LAG-3 fusion protein (LAG-3Ig), which is a first-in-class antigen presenting cell (APC) activator being explored in cancer. Immutep is also developing an agonist of LAG-3 (IMP761) for autoimmune disease.

Additional LAG-3 products, including antibodies for immune response modulation, are being developed by Immutep's large pharmaceutical partners.

Further information can be found on the Company's website www.immutep.com or by contacting:

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

U.S. Media:
Tim McCarthy, LifeSci Advisors
+1 (212) 915.2564; tim@lifesciadvisors.com

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

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