Press Release
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Immutep announces compelling clinical results from Phase II trial utilizing its first-in-class soluble LAG-3 protein, eftilagimod alpha, in first-line NSCLC at SITC 2022 Annual Meeting.

- **Overall response rate (ORR) increases to 40.4 percent, according to iRECIST, in TACTI-002 all-comer PD-L1 Phase II trial in first-line non-small cell lung cancer (1L NSCLC)**
- **ORR improved across all PD-L1 status groups by central assessment compared with data reported at ASCO 2022, including 48.3 percent, 44.7 percent, 55 percent, and 31.3 percent ORR in patients with PD-L1 TPS of greater than or equal to 1 percent, 1-49 percent, greater than or equal to 50 percent, and less 1 percent, respectively**
- **Interim median duration of response (DoR) of 21.6 months, compares favourably to historical controls including anti-PD-1 therapy combined with chemotherapy**
- **Despite approx 75 percent patients in trial having PD-L1 TPS less than 50 percent who are less likely to respond to anti-PD-1 monotherapy, promising results achieved in secondary endpoint of interim median Progression Free Survival (PFS) with overall PFS of 6.6 months and 9.3 months PFS in TPS greater than 1 percent**
- **Significant increase in IFN-γ and CXCL10 serum biomarkers for systemic TH1 response; substantiates efti's unique stimulation of the immune system also seen in the randomized AIPAC Phase IIb trial in Breast Cancer**

Sydney, Australia, November 10, 2022 – **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 compelling new clinical data from the TACTI-002 all-comer PD-L1 Phase II trial evaluating Immutep's lead product candidate, eftilagimod alpha ("efti" or "IMP321") in combination with MSD's (Merck and Co., Inc., Rahway, NJ., USA) anti-PD-1 therapy KEYTRUDA(R) (pembrolizumab) in 114 patients with 1L NSCLC.

The new data was presented today in a late-breaking abstract oral presentation (Abstract #1470) at the 37th Annual Society of Immunotherapy of Cancer (SITC) Meeting by Wade T. Iams, MD, Assistant Professor of Medicine, Vanderbilt-Ingram Cancer Center Division of Hematology/Oncology. Today's presentation followed the abstract data that had been discussed at the SITC 2022 Press Conference on 8 November 2022.

Dr. Iams stated, "The encouraging ORR, PFS and DCR presented today at SITC build on the promise of efti, a first-in-class soluble LAG-3 protein, to uniquely engage the innate and adaptive immune system to enhance the clinical effect of pembrolizumab. Responses in TACTI-002 were seen across all PD-L1 expression levels and histologic types, including in patients with PD-L1 TPS less than 50 percent. The deep and durable responses driven by efti plus pembrolizumab continue to be favorable with median DoR of 21.6 months."

Immutep CSO and CMO, Dr Frederic Triebel, noted, "The strengthening of efficacy, with improving overall response rates across all levels of PD-L1 stratification in first-line NSCLC patients, with no new safety signals, is quite encouraging. We are pleased to see ORR reach 40.4 percent, which compares favourably to the approximate 20 percent response rates in other PD-L1 all-comer trials utilizing anti-PD-1 monotherapy. Importantly, this additional clinical benefit is occurring with a safety profile consistent with that observed in previously reported studies for pembrolizumab monotherapy. We are also excited to share the first pharmacodynamic data from efti's combination with pembrolizumab, showing significant elevation of IFN-γ and the CXCL10 chemokine serum biomarkers for systemic TH1 response. Similar to the immune response biomarker data seen in efti's randomized Phase IIb trial in breast cancer, this further substantiates efti's novel ability to engage and activate the immune system."

Immutep CEO Marc Voigt added, "We are pleased to see patient outcomes improving yet again, and continue to believe that efti, with its unique mechanism of action targeting a subset of MHC class II

molecules to mediate antigen-presenting cell activation, holds significant potential to benefit cancer patients. This includes those with PD-L1 expression levels below 50 percent that represent the vast majority of patients with NSCLC. Based on this compelling data in this large Phase II trial, coupled with the large market opportunity and high unmet need for more durable and tolerable options, we continue to push forward with our late-stage clinical development plans in frontline NSCLC in combination with anti-PD-1 therapy."

Key Findings from TACTI-002 Phase II Trial in 1L NSCLC Patients (N=114) – Data cut-off date 1 July 2022:

- **Primary Endpoint** - The primary endpoint of overall response rate (ORR) by iRECIST increased to 40.4 percent in the TACTI-002 all-comer PD-L1 Phase II trial in 1L NSCLC
  - ORR improved across all PD-L1 status groups by central assessment compared with data reported at the American Society of Clinical Oncology's (ASCO) Annual Meeting in June 2022.
  - Encouraging ORR of 48.3 percent, 44.7 percent, 55.0 percent, and 31.3 percent was established in patients expressing a PD-L1 Tumor Proportion Score (TPS) of greater than 1 percent, 1-49 percent, greater than 50 percent, and less than 1 percent, respectively.
  - See Table 1 below
- **Secondary Endpoints** - Despite approx 75 percent of patients in the trial having PD-L1 TPS less than 50 percent, promising results were achieved in secondary endpoints of interim median Progression Free Survival (PFS) and Disease Control Rate (DCR):
  - Median PFS was 6.6 months overall and 9.3 months for patients with a PD-L1 TPS of greater than or equal to 1 percent, an increase from 8.4 months as reported at ASCO 2022.
  - DCR of 79.3 percent for patients with TPS of greater than 1 percent and improved for all PD-L1 groups except TPS less than 1 percent.
  - Of note, efti in combination with pembrolizumab has been granted Fast Track designation in combination with pembrolizumab in 1L NSCLC patients expressing PD-L1 TPS greater than or equal to 1 percent.
- **Duration of Response** - Deep and durable responses, with interim median DoR of 21.6 months, compares favourably to historical controls, including anti-PD-1 therapy combined with chemotherapy:
  - Response onset is early, and responses are long-lasting
  - Less than 10 percent of responding patients progress within 6 months
  - See Chart 2 below
- **Tumour Response by Tumor Type** - Comparable ORR and DCR for squamous (N=40, 37.5 percent ORR and 82.5 percent DCR) and non-squamous histologies (N=72, 40.3 percent ORR & 66.7 percent DCR)
- **Pharmacodynamic Analysis** - First pharmacodynamic data from efti plus pembrolizumab combination shows statistically significant increase in IFN-γ and CXCL10 serum biomarkers for systemic TH1 response, further substantiating efti's unique systemic stimulation of the immune system. This is similar to the biomarker analysis from Immutep's randomized AIPAC Phase IIb trial in metastatic breast cancer, which showed efti in combination with chemotherapy significantly increased the number of circulating immune cells (monocytes, activated CD8 T cells) and CXCL10 serum levels, compared to baseline. The increase in these pharmacodynamic markers (monocytes, CD8 T cells and CXCL10) was significantly linked to improved OS in the efti group, but not in the placebo group in the AIPAC trial.
- **Safety** - Treatment with efti plus pembrolizumab is safe and well-tolerated with no new safety signals, continuing the combination's favourable safety profile to date that is consistent with previously reported studies for pembrolizumab monotherapy. Only 9.6 percent of patients have discontinued due to adverse events related to study treatment, which is (1) in line with the data reported at ASCO 2022, (2) consistent with the discontinuation rate for pembrolizumab monotherapy, and (3) below historical discontinuation rates from other immunotherapy-immunotherapy & immunotherapy-chemotherapy combination trials.

Table 1 – Overall Response Rates - (data cut-off 1 July 2022)

	N, (ORR %)	95% CI*
Overall ORR as per iRECIST by local read *(primary endpoint)*		
ITT population	114, (40.4%)	[31.3-50.0]
Evaluable Patients	101, (45.5%)	[35.6-55.8]
ORR by PD-L1 Tumour Proportion Score (TPS)		
TPS <1%	32, (31.3%)	[16.1-50.0]
TPS 1-49%	38, (44.7%)	[28.6-61.7]
TPS ≥50%	20, (55.0%)	[31.5-76.9]
TPS ≥1%	58, (48.3%)	[35.0-61.8]

** 95% confidence intervals calculated using Clopper-Pearson method*

Chart 1 – Efficacy: Spider Plot

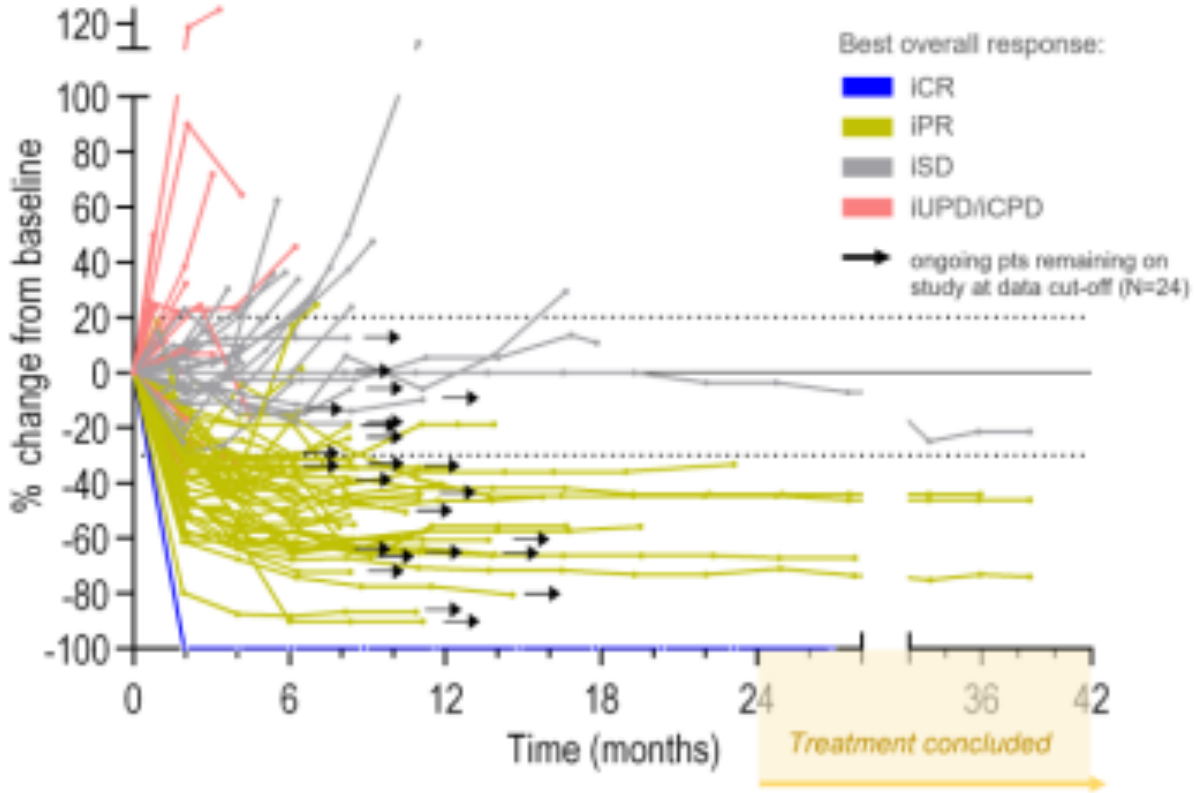
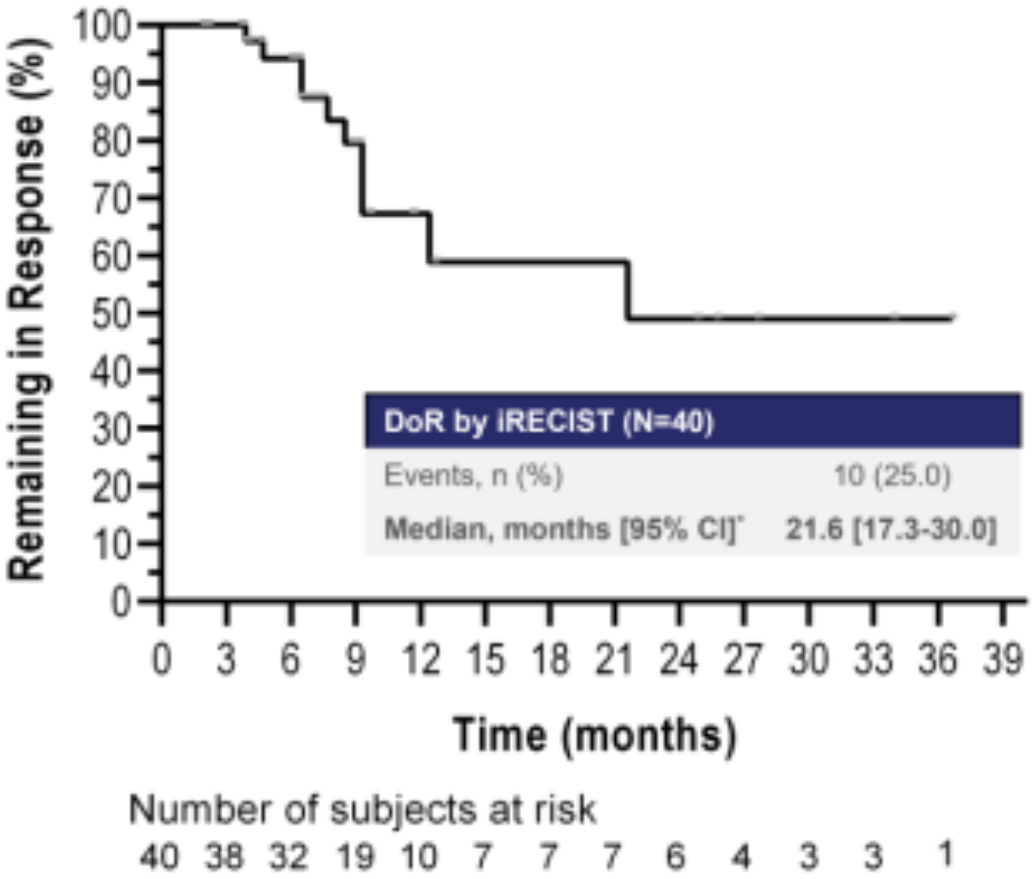


Chart 2 – Interim Duration of Response (DoR) by iRECIST



Trial endpoints
The primary endpoint was ORR according to iRECIST and local read. The data announced today represents the primary analysis of mature data of this endpoint. Secondary endpoints include ORR by RECIST 1.1 (consistent with iRECIST), DCR, DoR, PFS, Overall Survival (OS), and Safety assessments.

Patient population and condition
A total of 114 patients with 1L NSCLC were enrolled and treated with efti plus pembrolizumab in six countries across 19 trial sites throughout Europe, the United States, and Australia. Importantly, the patients were enrolled without any selection for PD-L1 status (PD-L1 all-comers), a biomarker indicating the likelihood of response to pembrolizumab. The trial was confirmed as a "PD-L1 all-comer trial" with approx 75 percent of patients having a Tumour Progression Score (TPS) of less than 50 percent. 99 percent of patients had metastatic disease at study entry and the patients had an ECOG performance status of 0 (37.7 percent) or 1 (62.3 percent). Treatment prior to study start included radiotherapy (33 percent), surgery (20 percent) and systemic therapy (23 percent) for non-metastatic disease. The trial reflects a typical patient population for this indication, including a mix of squamous/nonsquamous disease and male/female representation.

Conclusion
The combination of efti plus pembrolizumab is showing encouraging efficacy in 1L NSCLC patients across all PD-L1 status groups, including in PD-L1 low and PD-L1 negative patients. The combination is very well tolerated, and the low discontinuation rate is consistent with pembrolizumab monotherapy. The data support continued late-stage development in this indication.

Webcast
The Company will host a global webcast to discuss the new data from 1L NSCLC patients participating in its Phase II TACTI-002 trial including an analyst Q and A.

Details
Date and Time Thursday, 10 November 2022, at 5 pm U.S. ET / Friday, November 11, at 9 am Australian Eastern Daylight Time (AEDT)
Registration Webcast Link

Questions Investors are invited to submit questions in advance via immutep@citadelmagnus.com
Replay A replay will be available at www.immutep.com from the day after the event.

KEYTRUDA(R) is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ, USA.

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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 for the treatment of cancer, capitalising on LAG-3's unique characteristics to stimulate both innate and adaptive immunity. 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 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 first-line HNSCC and in first-line NSCLC from the United States Food and Drug Administration (FDA).

About the TACTI-002 Trial
TACTI-002 (Two ACTive Immunotherapies) is being conducted in collaboration with Merck and 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 anti-PD-1 therapy KEYTRUDA(R) (pembrolizumab) in patients with second-line head and neck squamous cell carcinoma or non-small cell lung cancer in the 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
• Part B - second-line NSCLC, PD-X refractory
• 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 clinical-stage biotechnology company leading the development of LAG-3-related immunotherapy products for the treatment of cancer and autoimmune disease. The Company is dedicated to leveraging its technology and expertise to bring innovative treatment options to market for patients and to maximise value to shareholders. Immutep's 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 in multiple clinical trials. The Company is also developing an agonist of LAG-3 (IMP761) for autoimmune disease. Additional LAG-3 product candidates, including antibodies for immune response modulation, are licensed to and being developed by Immutep's large pharmaceutical partners. Further information can be found on the Company's website www.immutep.com