ASX/Media Release

Immutep Publishes AIPAC, TACTI-002 and TACTI-003 Trial Posters at SITC with Positive New Data for LAG-3 Therapy, Eftilagimod Alpha

- **AIPAC** poster presentation includes new data and graphs showing:
  - Very encouraging Overall Survival (OS) data from the abstract published on 9 November 2021, including statistically significant benefit in 3 patient subgroups representing a majority of patients
  - A statistically significant Quality of Life preservation in first 6 months in the eftilagimod alpha ("efti") group in total population
  - The statistically significant increase in peripheral CD8 T cells in patients in the efti group of the total population[1] and the statistically significant correlation of this increase with improved OS
- **TACTI-002** poster presentation of more mature interim data from 2nd line head and neck squamous cell carcinoma (HNSCC) patients (Part C):
  - Encouraging Overall Response Rate (ORR), with 29.7% (11/37) of 2nd line HNSCC patients responding to the combination therapy of efti and pembrolizumab
  - Favourable duration and depth of responses, with 5 Complete Responses and a minimum duration of response extended to > 9 months across all responding patients
  - Responses continue to be seen in PD-L1 low and high expressors
  - Further data from TACTI-002 is expected to be reported in H1 calendar year 2022
- **TACTI-003** is a Phase IIb multicentre, open label, randomised and controlled, trial enrolling approximately 154 patients with 1st line HNSCC

SYDNEY, AUSTRALIA – 15 November 2021 – 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, announces new data has been published in poster presentations at the Society for Immunotherapy of Cancer (SITC) Annual Meeting 2021 which took place from 10-14 November 2021 in the US. The new data relates to the Company's Phase IIb AIPAC trial and Part C of its Phase II TACTI-002 study (also designated KEYNOTE-798). In addition, a poster presentation of the trial design of the Company's new randomised Phase IIb study in 1st line HNSCC was also presented at SITC.

All three poster presentations relate to Immutep's lead candidate efti and are available on the Company's website: https://www.immutep.com/investors-media/presentations.html. New data which is shown in addition to the data from the abstracts released on 9 November 2021 is summarised below.

Immutep will present data from the posters in a global webcast for investors on Wednesday, 17 November 2021 at 8.00 am AEDT / Tuesday, 16 November 2021 at 4.00 pm EST. Details are below.

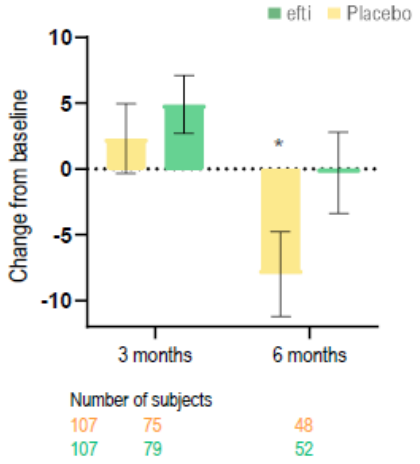
PHASE IIB AIPAC POSTER PRESENTATION

In addition to the final OS data announced on 10 November 2021, Immutep reports new Quality of Life (QoL) data from AIPAC. QoL is a secondary endpoint of the study. In the total trial population, a statistically significant QoL preservation was observed in the first 6 months in the efti group of patients who were treated with efti in combination with paclitaxel. This compares favourably to the comparator group (paclitaxel and placebo) where a significant deterioration in these measures were reported at 6 months

[1] Immune monitoring was conducted on a selection of patients from the total population: N=36/31 comparator group/efti group.

(see Figure 1). QoL is generally very important for patient compliance and forms part of reimbursement discussions after any potential marketing approval.

Figure 1. Quality of Life at 3 and 6 months of treatment (Global Health Status / QoL QLQC30-B23)[2]



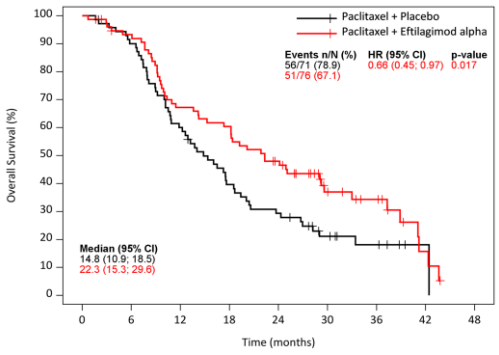
As previously announced, the AIPAC trial demonstrates a statistically significant and clinically meaningful OS benefit in now three prespecified (prior to unblinding) patient subgroups. A majority of patients fall into at least one of the patient subgroups and therefore derive a statistically significant benefit (Table 1).

- Patients under the age of 65 years (representing 66.7% of patients in the efti group) reported a median OS of 22.3 months compared to 14.8 months in the comparator group, indicating an absolute survival benefit of +7.5 months (HR = 0.66; p = 0.017) favoring the efti group (see Figure 2).

- Patients with a low monocyte count (< 0.25/nl) at the commencement of the study (representing 21.9% of patients in the efti group) reported a median OS of 32.5 months compared to 12.9 months in the comparator group, indicating an absolute survival benefit of +19.6 months (HR = 0.44; p = 0.008) favoring the efti group.

- Patients with a more proliferating tumor cell type expressing more neo-antigens (i.e. leading to more immunogenicity), characterised as luminal B (representing 48.8% of patients in the efti group) reported a median OS of 16.8 months compared to 12.6 months in the comparator group, indicating an absolute survival benefit of +4.2 months (HR = 0.67; p = 0.049) favoring the efti group.

Figure 2. Kaplan-Meier curve for OS in patients < 65 years of age



[2] * Differences are statistically significant.

Table 1 – Overall Survival in key patient subgroups at final analysis at 72.5% of events in the overall population

Group	% of patients in efti group	Efti group / Comparator group	Median OS (months)	Absolute OS benefit from efti
Total Population	100%	Efti + paclitaxel	20.4	**+2.9 months** HR = 0.88 p = 0.197
		Placebo + paclitaxel	17.5	
< 65 years	66.7%	Efti + paclitaxel	22.3	**+7.5 months** HR = 0.66 p = 0.017
		Placebo + paclitaxel	14.8	
Low monocytes < 0.25/nl	21.9%	Efti + paclitaxel	32.5	**+19.6 months** HR = 0.44 p = 0.008
		Placebo + paclitaxel	12.9	
Luminal B	48.8%	Efti + paclitaxel	16.8	**+4.2 months** HR = 0.67 p = 0.049
		Placebo + paclitaxel	12.6	

Pleasingly, these results have improved since interim data were reported at the San Antonio Breast Cancer Symposium (SABCS) in December 2020. A comparison is provided in Table 2.

Table 2 – Comparison of interim Overall Survival data and final Overall Survival data

Group	Interim data (SABCS 20)	Final data (SITC 21)	Median OS improvement [months]
Total Population	**+2.7 months** HR = 0.83 p = 0.14	**+2.9 months** HR = 0.88 p = 0.197	**+0.2**
< 65 years	**+7.1 months** HR = 0.62 p = 0.012	**+7.5 months** HR = 0.66 p = 0.017	**+0.4**
Low monocytes < 0.25/nl	**+9.4 months** HR = 0.47 p = 0.02	**+19.6 months** HR = 0.44 p = 0.008	**+10.2**
Luminal B	**+3.8 months** HR = 0.69 p = 0.077	**+4.2 months** HR = 0.67 p = 0.049	**+0.4**

In addition, as briefly reported on 10 November 2021, immune monitoring studies showed an increase in peripheral CD8 T cells in patients from the efti group of the total population (N=36/31 comparator group/efti group).[1] This increase is statistically significant and is also significantly correlated with improved OS, demonstrating strong proof-of-concept. New data and graphs are provided below (see Figures 3 & 4).

Figure 3. Mean ± SEM of absolute count of CD8 T cells* prior next dosing

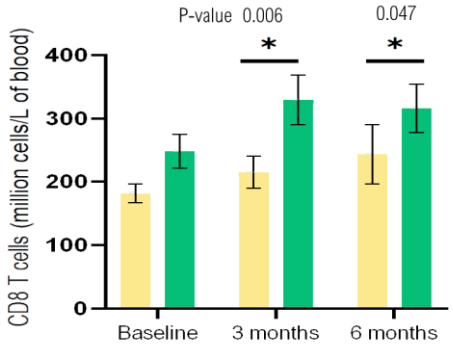
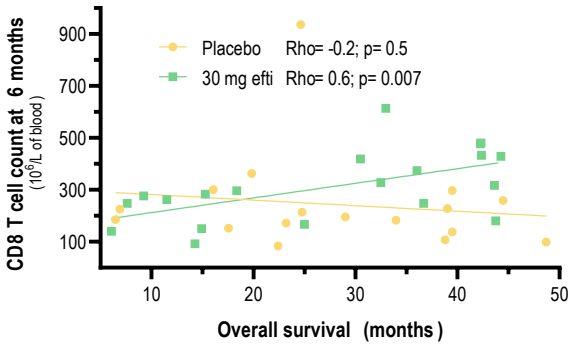


Figure 4. Correlation between cytotoxic CD8 T cells and OS



Immutep CEO, Marc Voigt commented: "The combination of the OS data in the prespecified subgroups, immune monitoring data and Quality of Life data, which were all statistically significant, give us confidence as we move forward with the development of efti in various late-stage settings. The results here are particularly noteworthy because $Her2^{-}HR^{+}$ metastatic breast cancer is not a particularly immunogenic tumour and so does not always respond to treatment with modern immunotherapies such as anti-PD-1 therapy. Indeed, we have seen across our various studies that efti, with its unique mechanism of action, has the potential to benefit many cancer patients, including those with more limited treatment options."

PHASE II TACTI-002 POSTER PRESENTATION

Immutep's TACTI-002 is being conducted in collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada). The study is evaluating the combination of efti with MSD's anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in 183 patients with non-small cell lung cancer (NSCLC) in 1st and 2nd line (Parts A and B, respectively) or 2nd line head and neck squamous cell carcinoma (HNSCC, Part C). The results announced today relate to Part C only.

Immutep CSO and CMO, Dr Frederic Triebel said: "It is encouraging to see deep and durable responses in low PD-L1 expressing patients who may not typically respond to anti-PD-1 therapy when given on its own. When given in combination with efti, we are seeing an ORR of about 30%. Results from TACTI-002 demonstrate an encouraging ORR combined with a durable response and good safety. This was key to securing Fast Track Designation with the US FDA in April this year."

Key Findings 2nd line HNSCC - Part C

- ORR of 29.7% (11/37) per iRECIST in patients unselected for PD-L1 on an intention-to-treat basis and 35.5% (11/31) in evaluable patients
- 13.5% of patients (5/37) reporting a Complete Response, indicating deep responses
- Median duration of response is not yet reached and none of the patients with a confirmed response progressed within 9 months
- 5 patients still under therapy and 1 patient completed 2 years of therapy
- ORR in patients in the PD-L1 ≥ 1 (N = 27) and PD-L1 ≥ 20 (N = 14) subgroups is 40.7% and 64.3%, respectively

Table 3 – TACTI-002 Interim ORR Results for Part C (data cut-off date: 4 August 2021)

	Part C 2nd line HNSCC[3]
Tumour Response Best Overall Response (BOR) per iRECIST	**Stage 1 & 2 N (%) Total N=37**
Complete Response (CR)	5 (13.5)
Partial Response (PR)	6 (16.2)
Stable Disease (SD)	3 (8.1)
Progressive Disease (PD)	17 (45.9)
Not Evaluable	6 (16.2)
Disease Control Rate (DCR)	**14 (37.8)**
Objective Response Rate (ORR)	**11 (29.7)**
ORR in evaluable pts (N=31)	**11 (35.5)**

Conclusion: The more mature data from 2nd line HNSCC patients continues to be encouraging, including when compared to historical studies with checkpoint inhibitor monotherapy in comparable patient groups. These results are supportive of Immutep's randomised Phase IIb TACTI-003 study in the 1st line HNSCC indication conducted in collaboration with MSD. The trial design for the new TACTI-003 study is outlined below.

Safety (data cut-off date 16 April 2021)
The combination treatment continues to be safe and well tolerated with no new safety signals reported thus far.

Next Results
Further data from TACTI-002 are planned to be reported in H1 of calendar year 2022.

PHASE II TACTI-003 POSTER PRESENTATION

TACTI-003 is a Phase IIb multicentre, open label, randomised and controlled, trial enrolling approximately 154 patients with 1st line HNSCC.

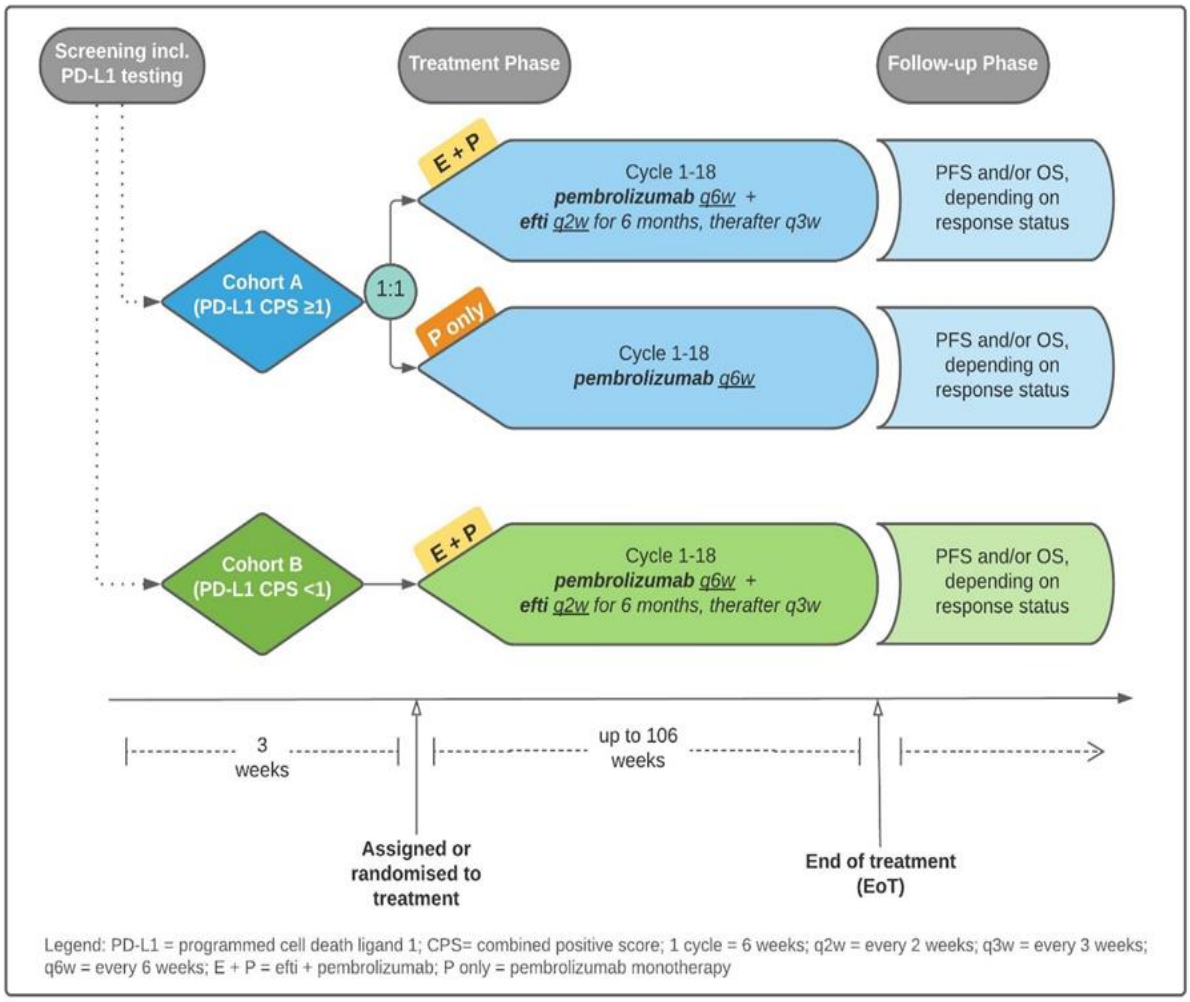
Patients will be enrolled into two cohorts (see Figure 5):

- Cohort A (approximately 130 patients) will evaluate the safety and efficacy of efti in combination with MSD's KEYTRUDA® (pembrolizumab), compared to pembrolizumab alone in 1st line metastatic or recurrent HNSCC patients with PD-L1 positive tumours (CPS ≥ 1).

- Cohort B (up to 24 patients) is an experimental arm which will determine the efficacy and safety of efti plus pembrolizumab in patients with PD-L1 negative tumours (CPS < 1).

[3] As assessed by local investigator read.

Figure 5. TACTI-003 trial design



Pembrolizumab will be given at a dose of 400 mg via intravenous infusion on day 1 of each 6-week treatment cycle (maximum of 18 infusions). Efti will be subcutaneously injected at a dose of 30 mg every 2 weeks for the first 6 months (4 cycles) and thereafter at a dose of 30 mg every 3 weeks for up to 2 years in total.

The primary endpoint of the study is ORR according to RECIST 1.1. and iRECIST will be used for treatment decisions. Secondary endpoints include OS and Progression Free Survival (PFS). The TACTI-003 study is open for patient recruitment in the US and Ukraine, with further clinical sites expected to be opened in the coming months.

GLOBAL WEBCAST

Date & Time: 8.00 am AEDT (Sydney) Wednesday 17 November 2021
4.00 pm EST (New York) Tuesday 16 November 2021
10.00 pm CET (Berlin) Tuesday 16 November 2021

Register: https://fnn.webex.com/fnn/onstage/g.php?MTID=ef12af93633b5d17a2e4e176fcac2f070

Questions: Investors are invited to submit questions in advance via immutep@citadelmagnus.com.

A replay of the webcast will also be available at www.immutep.com from the day after the event.

About AIPAC

Active Immunotherapy Paclitaxel (AIPAC) is a multicentre, placebo-controlled, double-blind, 1:1 randomised Phase IIb clinical trial in HER2-negative/HR positive metastatic breast cancer.

The study is evaluating the combination of efti with paclitaxel chemotherapy. 227 HER2-negative/HR positive metastatic breast cancer patients are randomised 1:1 to a chemo-immunotherapy arm (efti plus paclitaxel) or to a comparator arm (placebo plus paclitaxel). Patients receive weekly paclitaxel at days 1, 8 and 15, with either efti or placebo injected subcutaneously on days 2 and 16 of each 4-week cycle, repeated for 6 cycles. Thereafter, patients pass over to the maintenance phase with efti alone.

For more information regarding the AIPAC trial, visit clinicaltrials.gov (identifier: NCT02614833) and https://www.ncbi.nlm.nih.gov/pubmed/30977393.

About TACTI-002

TACTI-002 (Two ACTive Immunotherapies) is being conducted in collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada). The study is evaluating the combination of efti with MSD's KEYTRUDA® (pembrolizumab) in up to 183 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, the UK and US.

Patients participate in one of the following:

- Part A - first line non-small cell lung cancer (NSCLC), PD-X naive
- Part B - second line NSCLC, PD-X refractory
- Part C - second line head and neck squamous cell carcinoma (HNSCC), PD-X naive

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. PD-L1 expression is typically reported in three groups for NSCLC: < 1%, 1-49% and ≥ 50% (Tumour Proportion Score or TPS) and in HNSCC: < 1, 1-19 and ≥ 20 (Combined Positive Score or CPS). Patients with a high PD-L1 status are typically more responsive to anti-PD-1 therapy such as pembrolizumab, whereas those with low PD-L1 status are overall less responsive.

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

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

About TACTI-003

TACTI-003 is a Phase IIb clinical trial in first line head and neck squamous cell carcinoma (HNSCC) in collaboration with Merck & Co., Inc., Kenilworth, NJ, USA, known as "MSD" outside the United States and Canada. It will evaluate efti in combination with MSD's KEYTRUDA® (pembrolizumab) as a first line therapy in unresectable recurrent or metastatic HNSCC patients with PD-L1 negative and PD-L1 positive (CPS ≥ 1) tumours. It will be a randomised, controlled clinical study in approximately 154 first line HNSCC patients and will take place across Australia, Europe and the US in up to 35 clinical sites.

The study will evaluate the safety and efficacy of efti in combination with pembrolizumab, compared to pembrolizumab alone in first line metastatic or recurrent HNSCC patients with PD-L1 positive (CPS ≥ 1) tumours (cohort A), and determine the efficacy and safety of efti plus pembrolizumab in patients with PD-L1 negative tumours (CPS < 1) (cohort B). According to the current plans, about 130 patients in cohort A will be randomised 1:1 to receive either efti plus pembrolizumab or pembrolizumab alone. Subjects in cohort B (up to 24 patients) will receive a combination of efti and pembrolizumab.

The primary endpoint of the study is the Overall Response Rate (ORR) according to RECIST 1.1. and iRECIST will be used for treatment decisions. Secondary endpoints include OS and Progression Free Survival (PFS).

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 maximise value to shareholders.

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 and infectious disease. 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.

Immutep is listed on the Australian Securities Exchange (IMM), and on the NASDAQ (IMMP) in the United States.

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.