**ASX/Media Release**

# Immutep presents new and significant data from the AIPAC study

- Statistically significant increase in innate and adaptive immune response biomarkers (monocyte and CD8 T cell counts and serum CXCL10 levels) and absolute lymphocyte count (ALC) demonstrated in the efti group, but not in the placebo group
- The increase in pharmacodynamic markers is significantly linked to improved OS
- Exploratory analysis identified six patient subgroups with improvements in Overall Survival (OS) which are relevant for patient population selection for future late-stage studies
- Five of the six patient subgroups show a statistically significant improvement in OS

**SYDNEY, AUSTRALIA – 4 May 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, today reports new biomarker and exploratory analysis data from its Phase IIb AIPAC trial. The data was presented at ESMO's Breast Cancer Congress in a poster presentation which is available on ESMO's website and at https://www.immutep.com/investors-media/presentations.html.

The double blind and randomised AIPAC trial evaluated efti in combination with paclitaxel chemotherapy (efti group) compared to placebo plus paclitaxel (placebo group) in 227 patients with HER2-negative/HR positive metastatic breast cancer. Final OS results were reported in November 2021 in a late breaking abstract at SITC showing encouraging efficacy in multiple patient subgroups.

**Dr Frederic Triebel, Immutep's CSO and CMO said:** "The biomarker analysis is highly valuable for two key reasons. Firstly, the statistically significant difference in the immune response between the efti and placebo patients confirms efti is activating the immune system and helping patients live longer. This is demonstrated by the increase in circulating monocytes, CD8 T cells and a serum Th1 marker, CXCL10, plus the absolute lymphocyte count (ALC), and correlation of these improved immune parameters with overall survival. Secondly, the early rise in ALC in patients treated with efti provides clinicians with a potential predictor of improved survival, helping them to determine early on if continued treatment with efti is potentially beneficial."

"The exploratory analysis showing statistically significant improvements in OS in different patient subgroups is also very important as we work towards the optimal design of the planned registrational trial in breast cancer. This all continues to be consistent with our long-held belief that efti, with its unique mechanism of action, should be able to help diverse sets of patients, including those who fail to respond to current immunotherapy options," he concluded.

**Increase in immune response biomarkers linked to improved overall survival**

Biomarker analysis showed efti, in combination with weekly paclitaxel, significantly increased the number of circulating immune cells (monocytes, activated CD8 T cells) and CXCL10 serum levels, compared to baseline. The increase was not observed in the placebo group (see Table 1). An increase in activated CD4 cells was also observed. 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. These findings of an improved immune status are also relevant for the anti-PD-1 combinations with efti.

Notably, in the biomarker study, patient blood samples were drawn 13 days after efti injection. This was to ensure that the study would show the minimum residual pharmacodynamic effect from therapy with efti and paclitaxel, since efti disappears from the blood in only 3-4 days.

Thus, since efti is administered every 14 days, we conclude that that the observed increase in the number of circulating immune cells was sustained throughout the course of treatment (or even greater at the peak of the immune response).

**Potential predictive biomarker for improved survival**

The absolute lymphocyte count (ALC) was shown to increase early and sustainably in patient's treatment regimen in the efti group, but not the placebo group. The increase in ALC was also significantly linked to improved OS. ALC can be measured easily in every hospital laboratory, making it a practical potential predictive biomarker for efti efficacy and therefore improved survival.

***Table 1. Immune response biomarkers compared to placebo***

| Biomarker | Treatment | Fold change mean ± SEM<br>Median | p-value (2-sided rank-sum Wilcoxon test) |
|---|---|---|---|
| **Monocytes** | Efti (n = 42) | 5.81 ± 1.49<br>2.07 | 0.025 |
| | Placebo (n = 34) | 2.29 ± 0.44<br>1.47 | |
| **Activated CD8 T cells** | Efti (n = 42) | 2.54 ± 0.35<br>1.76 | 0.027 |
| | Placebo (n = 34) | 1.86 ± 0.40<br>1.17 | |
| **CXCL10** | Efti (n = 32) | 2.78 ± 0.30<br>2.39 | 0.006 |
| | Placebo (n = 22) | 1.56 ± 0.18<br>1.40 | |

**Univariate and multivariate analysis indicates subgroups for future studies**

Through exploratory analyses, six subgroups of patients showed an improvement in OS in the efti group, compared to placebo (see Table 2). Five of the six subgroups (< 65 years, low baseline monocytes, high neutrophil to lymphocyte ratio (NLR), < 5 years since diagnosis and luminal B) showed a statistically significant improvement in OS and in the 'no prior taxane therapy subgroup' a statistically significant increase was also seen in ORR.

The subgroups will be considered for patient population selection for future studies, such as Immutep's planned Phase III AIPAC-003 trial.

Multivariate analysis showed patients entering the trial with high body mass index (BMI) and prior CDK4/6 treatment had significantly poorer PFS and OS outcomes irrespective of the therapy they received. High BMI and prior CDK4/6 treatment are therefore considered independent poor prognostic markers and will be considered as stratification factors for future studies. Multivariate analysis also showed that low monocytes and no prior taxane therapy were independent significant predictive factors for improved OS.

***Table 2. Six favourable subgroups with improved OS based on univariate analysis***

| Subgroup | Absolute gain in median Overall Survival (months) (hazard ratio, p value) |
|---|---|
| **< 65 years** | +7.5 (0.66, 0.017) |
| **Low baseline monocytes** | +19.6 (0.44, 0.008) |
| **High neutrophil to lymphocyte ratio (NLR)** | +6.9 (0.61, 0.012) |
| **< 5 years since diagnosis** | +4.8 (0.62, 0.025) |
| **Luminal B** | +4.2 (0.67, 0.049) |
| **No prior taxane therapy** | +4.8 (0.74, 0.076) |

**About the AIPAC Trial**

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

The study evaluated the combination of Immutep's lead product candidate, eftilagimod alpha (efti, LAG-3Ig or IMP321), and paclitaxel chemotherapy. 227 HER2-negative/HR positive metastatic breast cancer patients were randomised 1:1 to a chemo-immunotherapy arm (efti plus paclitaxel) or to a comparator arm (placebo plus paclitaxel). Patients received 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 passed 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 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'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:

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