

ASX/Media Release

## Immutep Reports Statistically Significant Survival Benefit for Key Patient Groups in the Ongoing Phase IIb AIPAC Study in Metastatic Breast Cancer

- First time an antigen presenting cell (APC) activator has shown an Overall Survival (OS) benefit in a randomised setting in metastatic breast cancer patients known to be insensitive to immune checkpoint inhibitor therapy
- Promising and improving overall trend in OS in total population (based on approx. 60% of events): median survival benefit of +2.7 months from efti plus chemotherapy, compared to chemotherapy plus placebo
- Statistically significant OS benefit in efti group observed in pre-defined patient groups:
  - **+7.1 months survival benefit** (median of 21.9 vs. 14.8 months, nearly 50% longer) from efti with chemotherapy for patients under 65 years of age
  - **+9.4 months survival benefit** (median of 22.4 vs. 12.9 months, 74% longer) from efti with chemotherapy for patients with a low starting monocyte count
- Statistically significant increase in CD8 T cells in patients treated with efti plus chemotherapy, correlated with prolonged OS, indicating pharmacodynamic activity and proof of concept of efti's mode of action
- Collection of OS data ongoing, with final data expected to be reported mid 2021
- Investor webcast to discuss survival data scheduled for Friday, 11 December 2020, at 8.30 am Australian Eastern Daylight Time, details below

**SYDNEY, AUSTRALIA – 10 December 2020 – Immutep Limited** (ASX: IMM; NASDAQ: IMMP) a biotechnology company developing novel immunotherapy treatments for cancer and autoimmune disease, is pleased to report encouraging first Overall Survival (OS) follow up data from its ongoing Phase IIb AIPAC study evaluating Immutep's lead product candidate eftilagimod alpha in combination with paclitaxel chemotherapy ("efti group") in comparison to a combination of placebo and paclitaxel chemotherapy ("comparator group") in patients with HER2-negative/HR positive metastatic breast cancer (HR+ MBC). These data were selected to be presented in a spotlight presentation at the San Antonio Breast Cancer Symposium 2020, which is being held virtually this week from Texas, USA.

**AIPAC Principal Investigator, Hans Wildiers of University Hospital Leuven, Leuven, Belgium, said:**

"Improving Overall Survival is a key endpoint when evaluating the benefit of new anticancer drugs. Efti is a new drug targeting the immune system in an innovative way and has the potential to improve outcomes in HER2-negative/hormone receptor positive metastatic breast cancer patients. The AIPAC study investigated efti in combination with first line chemotherapy in this population, a group of about 250,000 patients diagnosed worldwide each year. Although the progression free survival data in the efti group did not show a significant improvement versus the comparator arm in AIPAC earlier this year, the OS data in general looks already very interesting and will mature further. The OS data in subgroups such as those below age 65 years are highly encouraging and may lead to more effective treatment options for metastatic breast cancer patients."

**Immutep CSO and CMO, Dr Frederic Triebel said:** "We are very excited to see that efti is boosting the immune system by providing a statistically significant increase in CD8 T cell numbers, which is correlated with prolonged survival for patients. These data provide proof-of-concept and support our long-held belief that efti can provide a meaningful benefit to patients in a range of cancer settings by "pushing the

gas” on the body’s immune system, representing an important landmark. Through this mechanism, efti is helping a large proportion of patients in the AIPAC study with Her2-HR+ metastatic breast cancer which is typically a non-immunogenic cancer and is therefore significantly less responsive to modern immune checkpoint inhibitor (ICI) therapies. As such, chemotherapy continues to be the standard of care in many instances and there continues to be a large unmet medical need. We look forward to reporting final survival data in 2021.”

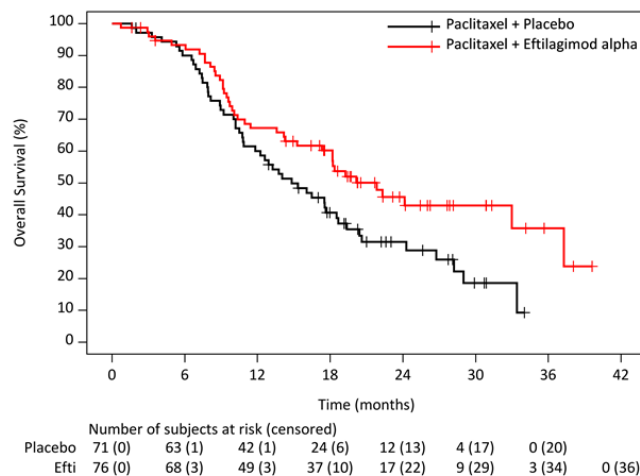
**Immutep CEO, Marc Voigt said:** “AIPAC marks an important milestone for Immutep and builds our confidence that efti is beneficial for many cancer patients, including those with metastatic breast cancer. Notably, we have seen a more material OS benefit than PFS benefit in this study; however, we note that this is not unusual for some immunotherapies where it can take time for the body’s immune system to be boosted and provide a therapeutic benefit. We are very encouraged by these first OS results which, subject to ongoing data collection, warrant a registrational perspective and regulatory interactions towards what we hope will be an important new class of medicines.”

**Key Efficacy Results: data cut-off 24 September 2020**

In the total patient population, first OS data (based on approx. 60% of events) show that patients in the efti group had an improving OS trend with a median OS of 20.2 months compared to 17.5 months for patients in the comparator group, indicating a survival benefit of +2.7 months (HR = 0.83; p = 0.14). The OS analysis is based on a 2-sided false positive probability of 0.05. Furthermore, a significant deterioration in quality of life was observed for patients in the comparator group at week 25, which was not observed in the efti group. This is an encouraging observation as these types of benefits are supportive of efti being eligible for reimbursement upon marketing approval.

In key predefined patient groups, the study has already demonstrated a statistically significant and clinically relevant OS benefit from treatment with efti in combination with chemotherapy. Patients under the age of 65 years (representing 66.7% of patients in the efti group) reported a median OS of 21.9 months compared to 14.8 months in the comparator group, indicating a survival benefit of +7.1 months (HR = 0.62; p = 0.012) favoring the efti group.

Figure 1 – Kaplan Meyer curve OS for patients < 65 years



The current data suggest that for patients younger than 65 years old, the probability of being alive at three years with efti plus chemotherapy vs. chemotherapy alone is increased by 100%.

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Furthermore, patients with a low monocyte count at baseline (representing 21.9% of patients in the efti group) reported a median OS of 22.4 months compared to 12.9 months in the comparator group, indicating a survival benefit of +9.4 months (HR = 0.47; p = 0.02) favoring the efti group.

Trending towards statistical significance, patients with a more aggressive, more immunogenic luminal B type of breast cancer (representing 48.8% of patients in the efti group) reported a median OS of 16.3 months compared to 12.6 months in the comparator group, indicating a beneficial trend of +3.8 months (HR = 0.69; p = 0.077) favoring the efti group. (See Table 1)

Table 1 – Overall Survival in key patient groups

Group	% of patients in efti group	Efti group / Comparator group	Median OS (months)	Absolute OS benefit from efti
Total Population	100%	Efti + paclitaxel	20.2	<b>+2.7 months</b> HR = 0.83 p = 0.14
		Placebo + paclitaxel	17.5	
< 65 years	66.7%	Efti + paclitaxel	21.9	<b>+7.1 months</b> HR = 0.62 p = 0.012
		Placebo + paclitaxel	14.8	
Low monocytes < 0.25/nl	21.9%	Efti + paclitaxel	22.4	<b>+9.4 months</b> HR = 0.47 p = 0.02
		Placebo + paclitaxel	12.9	
Luminal B	48.8%	Efti + paclitaxel	16.3	<b>+3.8 months</b> HR = 0.69 p = 0.077
		Placebo + paclitaxel	12.6	

**Note:** A lower HR, means a reduced risk of death, e.g. by 53% in the low monocyte group.

### Immuno Monitoring Results

Importantly, there was a statistically significant, sustained long-term increase in peripheral CD8 T cells in patients in the efti group. This is consistent with the mode of action of efti. There was also a statistically significant correlation between those patients having an increase in the number of CD8 T cells and those having a prolonged OS. This represents a strong proof-of-concept in a randomised, double blinded setting.

### Safety

The combination of efti and paclitaxel chemotherapy was overall safe and well tolerated, further building upon efti's strong safety profile to date.

The presentation poster is available at [www.immutep.com/investors-media/presentations.html](http://www.immutep.com/investors-media/presentations.html).

### Next Steps

Multivariate analysis of the data is ongoing and final OS data is expected to be reported in mid 2021.

### Webcast Details

Immutep will present this AIPAC data in a global webcast for investors, details are as follows:

- Date & Time: Friday, 11 December 2020, at 8.30 am Australian Eastern Daylight Time (AEDT) (Thursday, December 10<sup>th</sup>, at 4:30 p.m. U.S. ET)
- Register: <http://public.viavid.com/index.php?id=142664>

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- Questions: Investors are invited to submit questions in advance via [immutep@citadelmagnus.com](mailto:immutep@citadelmagnus.com).

A replay of the webcast will also be available at [www.immutep.com](http://www.immutep.com) from the day after the event.

#### **About the AIPAC trial**

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 Immutep's lead product candidate, eftilagimod alpha (efti, LAG-3Ig or IMP321), and 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](http://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 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 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.

Further information can be found on the Company's website [www.immutep.com](http://www.immutep.com) or by contacting:

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