immutep
LAG-3 IMMUNOTHERAPY

Investor Update

November 2024

The Opportunity Ahead as a Phase III Biotech Targeting First Line Treatment of Non-Small Cell Lung Cancer

IN THIS ISSUE

Message from the CEO

Since prioritising first line non-small cell lung cancer (1L NSCLC) within our late-stage clinical strategy two years ago, Immutep is now on the verge of becoming a Phase III biotech company. Our journey to this point has been led by our lead clinical candidate eftilagimod alpha's (efti) ability to safely enhance clinical outcomes and expand the number of patients who respond to standard-of-care therapies, including anti-PD-1 therapy, chemotherapy, and radiotherapy. The selection of 1L NSCLC as our focus indication was driven by compelling clinical results achieved with efti, coupled with the large market opportunity and high unmet need for more durable options. The data that has emerged in our lung cancer trials since has only increased our confidence in this decision.

"The potential for efti in combination with KEYTRUDA and chemotherapy is to set a new standard-of-care 1L NSCLC. We are confident in efti's ability to strengthen clinical outcomes and expand the number of patients who respond to the world's top selling drug."

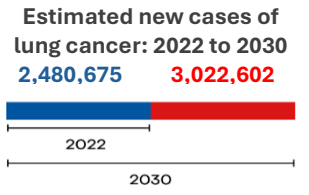
We are now in the fortunate position to have efti being evaluated in combination with the top selling drug in the world (KEYTRUDA®) targeting one of the largest indications in oncology, 1L NSCLC, in a Phase III. This is due to our third and most important collaboration with MSD (Merck & Co) signed in June 2024. With an estimated ~35% of KEYTRUDA's $28 billion in trailing twelve-month sales[1] from lung cancer (predominantly 1L NSCLC), a successful outcome in the upcoming TACTI-004 (**T**wo **ACTI**ve **I**mmunotherapies) trial would present a blockbuster opportunity for efti. Importantly, unlike many new drugs that must establish themselves in markets, efti will be uniquely positioned as an "add-on" to KEYTRUDA in combination with chemotherapy, the leading standard-of-care treatment in 1L NSCLC today.

Among the topics this update will cover are Immutep's favourable positioning as a Phase III company in one of the largest markets in oncology and the pivotal TACTI-004 trial designed in collaboration with MSD. The design of TACTI-004 sets the foundation for efti in combination with KEYTRUDA and chemotherapy to potentially establish a new standard-of-care for almost all 1L NSCLC patients eligible for anti-PD-1 therapy.

Before moving on, I would like to thank all our shareholders for their support. We are in a strong financial position with cash runway to the end of CY2026 to reach multiple catalysts and milestones to create shareholder value as we strive to make a positive difference in the lives of cancer patients globally.

Non-Small Cell Lung Cancer: Over 2 Million Cases Annually and Growing; High Unmet Need

Lung cancer is the leading cause of death among all cancer types and the incidence is set to increase to approximately 3 million cases worldwide by 2030[2]. NSCLC is the most common type of lung cancer representing ~80-85% of all diagnoses.[3] While immune checkpoint inhibitors (ICI) like anti-PD-1 therapy have revolutionised treatment of 1L NSCLC, only ~20% of patients respond to ICIs alone driving substantial research in combination therapies to

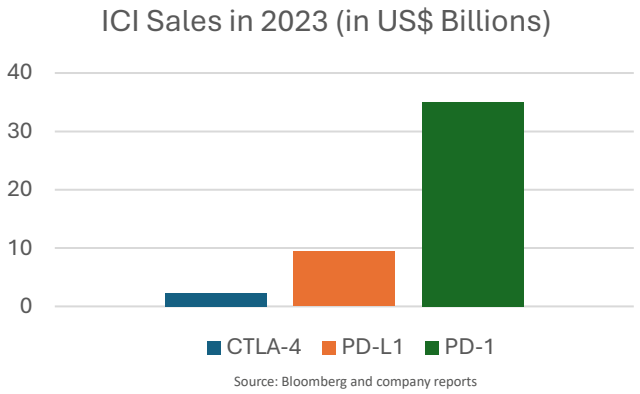


Source: Int'l Agency for Research on Cancer – WHO

generate better response rates and clinical outcomes. The condition is often diagnosed at a late stage[4], and less than 30% of patients are alive five years after diagnosis[5]. Given these facts, there remains a high unmet need for additional treatment options for people living with NSCLC.

Standard-of-Care KEYTRUDA and its Dominant Market Share in Metastatic Lung Cancer

Immune checkpoint inhibitors (ICI) have revolutionised the treatment landscape for many cancer types. As shown in the graphic, the most widely used ICIs are anti-PD-1 therapies[6], which also have the highest estimated growth rate in the years ahead. Among these PD-1 inhibitors KEYTRUDA is dominant, capturing ~71% of the roughly $35 billion of anti-PD-1 therapeutics sold in 2023.



Today, KEYTRUDA has approvals in over 40 cancer indications[7] and the most significant is lung cancer. It represented an estimated $9 billion of KEYTRUDA's $25 billion in sales during 2023[8]. To put KEYTRUDA's dominance in lung cancer into perspective, MSD captures between 7 to 8 of every 10 metastatic lung cancer patients today[9].

With this said, the sheer size of the 1L NSCLC market is such that multiple ICI-based approaches are successful commercially. Estimates have the total addressable NSCLC drug market rising to US$48 billion in sales in 2031 and ICIs generating over half those sales[10]. Which ICIs have approvals as monotherapy or in combination to treat lung cancer are often based on PD-L1 expression as measured by tumour proportion score (TPS). This FDA-approved biomarker for PD-1/PD-L1 inhibitors in metastatic 1L NSCLC stratifies patients into three key PD-L1 levels: high (TPS ≥50%), low (TPS 1-49%), and negative (TPS <1%).

Each of these PD-L1 levels represents approximately one-third of the total 1L NSCLC patient population, making one segment just as valuable as the others. Another stratification factor for ICI therapy is whether a patient has non-squamous (NSQ) or squamous (SQ) cancer types, representing roughly 70% and 30% of 1L NSCLC cases, respectively.

The table below shows the regulatory approvals for ICIs in the US and EU for the treatment of 1L NSCLC either as monotherapy or in combination with another immunotherapy and/or chemotherapy[11]:

1L NSCLC ICI Therapies	**High PD-L1 (TPS ≥50%)**				**Low PD-L1 (TPS 1-49%)**				**Negative PD-L1 (TPS<1%)**			
	US		EU		US		EU		US		EU	
Non-Squamous/Squamous (NSQ/SQ)	*NSQ*	*SQ*	*NSQ*	*SQ*	*NSQ*	*SQ*	*NSQ*	*SQ*	*NSQ*	*SQ*	*NSQ*	*SQ*
KEYTRUDA + Chemo	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
OPDIVO + Yervoy + Chemo	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
LIBTAYO + Chemo	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗
OPDIVO + Yervoy	✓	✓	✓	✓	✓	✓	✗	✗	✗	✗	✗	✗
KEYTRUDA Monotherapy	✓	✓	✓	✓	✓	✓	✗	✗	✗	✗	✗	✗
LIBTAYO Monotherapy	✓	✓	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
TECENTRIQ Monotherapy	✓	✓	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
TECENTRIQ + Bev + Chemo	✓	✗	✓	✗	✓	✗	✓	✗	✓	✗	✓	✗

The largest commercial market opportunity in 1L NSCLC captures all patients regardless of PD-L1 expression (TPS 0-100%) as well as both NSQ and SQ cancer types, and it is this patient population that KEYTRUDA in combination with chemotherapy is most often chosen by physicians today.

TACTI-004 is designed to target this exact same large patient population and based on the efficacy and safety results achieved to date, efti in combination with KEYTRUDA and chemotherapy is uniquely positioned to potentially drive a new standard-of-care treatment paradigm.

A Differentiated Approach in Metastatic 1L NSCLC with Efti, a First-in-Class MHC Class II Agonist

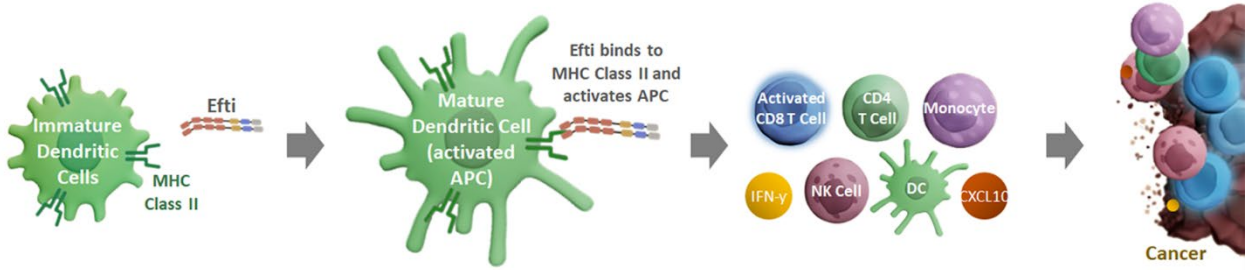
What sets efti apart from all other cancer immunotherapies is (1) it is a first-in-class soluble LAG-3 protein and (2) it is the only MHC Class II agonist in clinical development today. Quite simply, there is nothing else like it.

Immutep uses this proprietary LAG-3 immunotherapy as a tool to stimulate a broad anti-cancer immune response through its unique activation of antigen-presenting cells (APC) known as dendritic cells.

The discovery of these powerful immune cells by Rockefeller University scientist Ralph M. Steinman in 1973 led to his 2011 Nobel Prize in Physiology or Medicine[12]. In Rockefeller University's overview of Dr. Steinman's accomplishment, the dendritic cell is described as *"the cell type that is almost singularly responsible for commanding the efforts of all other immune cells"*.

As master regulators of the immune response, dendritic cells represent the key bridge between adaptive and innate immunity, and they play an essential role in orchestrating an effective response against cancer[13]. Efti flips the "on switch" to these powerful immune cells by binding to a specific subset of MHC class II molecules. This leads to the activation and proliferation of cytotoxic CD8+ T cells, CD4+ helper T cells, dendritic cells, NK cells, and monocytes to target and kill cancer.

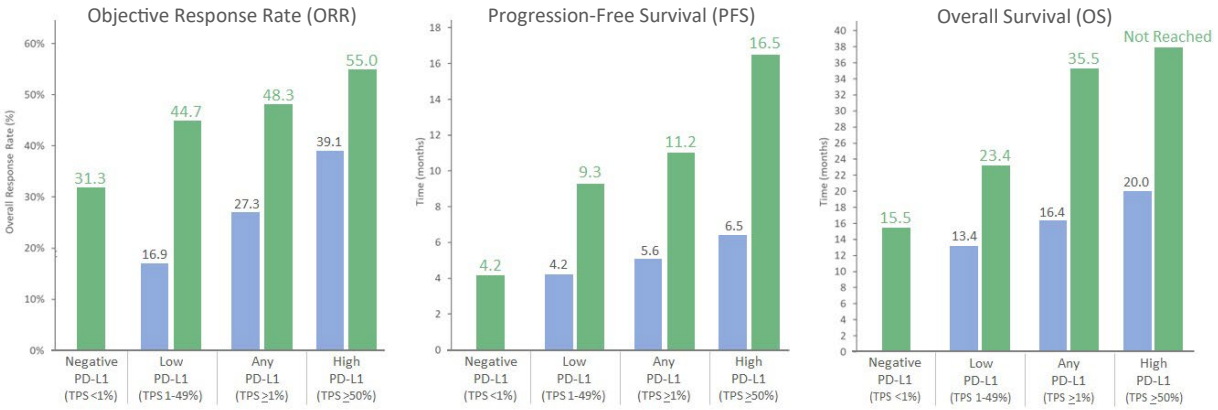
Additionally, efti upregulates the expression of key biological molecules including C-X-C motif chemokine ligand 10 (CXCL10) that recruits cancer-fighting immune cells to tumour sites and interferon-gamma (IFN-γ), which enhances the function of cytotoxic CD8+ T cells and further boosts their anti-tumour effects. This is all achieved via simple subcutaneous administration of efti, which provides a better patient experience and broadens access for patients and healthcare providers alike as compared to intravenous administration.



Immutep's differentiated immuno-oncology (IO) approach is leading to the alignment of efficacy and safety with mature clinical data in multiple clinical trials focused on 1L NSCLC. Importantly, efti in combination with KEYTRUDA with or without chemotherapy has led to very strong response rates and durable responses across all levels of PD-L1 expression in patients with 1L NSCLC. More importantly, the impressive

response rates, durability, and progression-free survival (PFS) achieved in these 1L NSCLC trials has translated into compelling overall survival (OS) as well.

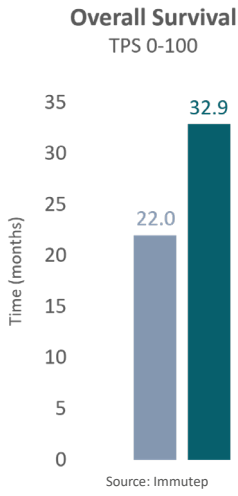
Robust response rates, durability, and progression free survival from efti plus pembrolizumab across all PD-L1 expression levels translate into compelling overall survival



Source: Immutep Corporate Presentation

This has been seen across two clinical trials in 1L NSCLC evaluating efti with KEYTRUDA. The first trial is the relatively large TACTI-002 Phase II (data shown above)[14] with 114 patients enrolled across six different countries. Data from this trial have previously been selected for oral presentations at three prestigious conferences: ESMO, SITC, and ASCO. The second trial is the investigator-initiated INSIGHT-003 Phase I evaluating efti + KEYTRUDA + chemotherapy that's enrolling patients at several top institutions in Germany.

As reported on 14 November 2024, mature data from patients in INSIGHT-003 with a minimum follow-up of 22 months (N=21) shows excellent results that exceeded expectations with ***32.9 months median OS***, 12.7 months median PFS, and 24-month OS rate of 81.0%[15]. These compare favourably to the ***22.0-month median OS***, 9.0-month median PFS, and 24-month OS rate of 45.5% from a registrational trial of anti-PD-1 and doublet chemotherapy, which also enrolled non-squamous 1L NSCLC patients regardless of PD-L1 expression[16].



Source: Immutep

Notably, only ~19% of the 21 patients in INSIGHT-003 with mature survival data have high PD-L1 expression, who typically respond better to anti-PD-1 therapy, versus ~32% in the registrational trial of anti-PD-1 and doublet chemotherapy[17]. INSIGHT-003's skew towards patients with negative (TPS <1%) and low (TPS 1-49%) PD-L1 expression further underpins the strength of the data we are seeing from the study.

Data from all evaluable patients in INSIGHT-003 through the 15 October 2024 cutoff date (N=40) demonstrates significant improvement of Objective Response Rate (ORR) according to RECIST 1.1 across all levels of PD-L1 expression compared to historical control[15,16]. In patients with low and negative PD-L1 expression (36 of 40 patients), who are typically less responsive to anti-PD-1 therapy, the triple combination achieved a 52.8% ORR and 86.1% Disease Control Rate (DCR). Of note, all 19 patients in the expansion cohort have TPS <50% and several with stable disease have potential to become responders.

Additional data updates from INSIGHT-003 are expected in 2025 and beyond.

Strategic Collaboration with MSD for Phase III Trial in First Line Non-Small Cell Lung Cancer

While ICIs have revolutionised the treatment landscape in NSCLC, most patients do not respond to anti-PD-(L)1 monotherapy. This has driven the biotech industry to search for combinations with anti-PD-(L)1 therapies that can (1) expand the number of patients who respond, (2) improve upon the clinical outcomes for patients who do respond, and (3) overcome primary or acquired resistance. Efti's clinical data to date in 1L NSCLC suggests it can accomplish all of these in combination with anti-PD-1 therapy in a safe manner.

In June 2024, Immutep entered into a clinical trial collaboration and supply agreement with MSD (Merck & Co., Inc., Rahway, NJ, USA), through a subsidiary, to evaluate efti in combination with MSD's anti-PD-1 therapy KEYTRUDA® and chemotherapy for the first-line treatment of metastatic NSCLC in a pivotal Phase III trial[16]. At its signing, this collaboration and supply agreement was the first for a Phase III that MSD had entered into in over two years.

This triple combination therapy with efti has the potential to set a new standard-of-care across the entire NSCLC patient population regardless of PD-L1 expression by strengthening clinical outcomes for responders, overcoming primary resistance, and broadening the number of patients who respond to therapy.

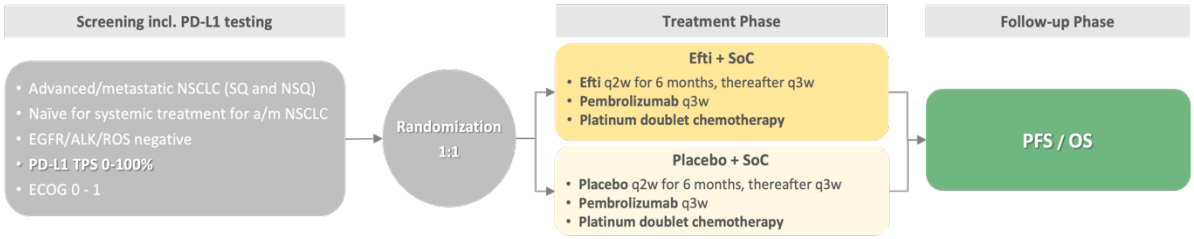
TACTI-004 Phase III

- **Third and most important collaboration & supply agreement with MSD signed in June 2024**
- **Registrational Phase III trial in 1L NSCLC with ~750 patients**
- **Immutep to conduct trial & retains all commercial rights to efti**
- **Potential to establish new standard-of-care in NSCLC, one of largest oncology indications and revenue drivers for KEYTRUDA**
- **Planned KEYTRUDA supply has significant value (typical ICI drug supply for such a PIII trial is approx. US$100m)**

TACTI-004 (Two ACTive Immunotherapies-004) Registrational Phase III Trial

TACTI-004 will be a 1:1 randomised, double-blind, multinational, controlled clinical study to evaluate efti in combination with MSD's KEYTRUDA® (pembrolizumab) and standard chemotherapy compared to the combination of pembrolizumab, chemotherapy and placebo in first-line metastatic NSCLC, regardless of PD-L1 expression, not amenable to EGFR/ALK/ROS1 based therapy. The global study will enrol ~750 NSCLC patients, including non-squamous/squamous subtypes, in more than 150 sites and well over 20 countries worldwide.

TACTI-004 / KEYNOTE-PNC-91 Trial Design



The trial design was formulated in collaboration with MSD and has received positive feedback from the US FDA and other regulatory agencies. Overall Survival (OS) and Progression-Free Survival (PFS) are dual primary endpoints, and like most large pharma Phase III trials, a reasonable differential between treatment and control arms will lead to the trial's success.

Importantly, the trial also has a prespecified futility boundary in late 2025 or early 2026 and a preplanned

interim analysis that could occur as soon as year-end 2026 or early 2027 depending on events. Both are key milestones.

Summary

In summary, we are excited as we approach the initiation of the TACTI-004 registrational trial and becoming a Phase III company.

The largest commercial market opportunity in 1L NSCLC captures all patients regardless of PD-L1 expression (TPS 0-100%) as well as both non-squamous and squamous cancer types. It is this patient population that KEYTRUDA in combination with chemotherapy is most often chosen by physicians today. TACTI-004 targets this exact patient population. This is key because if the Phase III trial is successful, efti will be positioned as a simple "add-on" to KEYTRUDA in combination with chemotherapy that does billions of dollars in sales in 1L NSCLC today.

We have high confidence in efti's ability to strengthen clinical outcomes and expand the number of lung cancer patients who respond to the world's top selling drug. This belief is bolstered by the strength of efficacy and safety results achieved to date across two lung cancer trials evaluating efti with KEYTRUDA, and particularly as it relates to TACTI-004's dual primary endpoints of Overall Survival and Progression-Free Survival. Like most large pharma Phase III trials, a reasonable differential between treatment and control arms would lead to the trial's success.

We are grateful for the continued support of our shareholders and investors that has provided us with strong financial means to advance our plan to make a lasting difference in the lives of cancer patients and their families worldwide.

Footnotes:

1. *Source of sales figures: Bloomberg, Wall Street research reports and Company reports.*
2. *International Agency for Research on Cancer – World Health Organization. Rates of trachea, bronchus and lung cancer.*
3. *Zappa C & Mousa Non-small cell lung cancer: current treatment and future advances, Transl Lung Cancer Res. 2016 Jun; 5(3): 288–300.*
4. *Polanco D et al. Prognostic value of symptoms at lung cancer diagnosis: a three-year observational study. J Thorac Dis 2021;13:1485–1494.*
5. *National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) https://seer.cancer.gov/statfacts/html/lungb.html*
6. *Bloomberg and company reports; Currency: USD. 2023 sales of approved anti-PD-1 therapies include pembrolizumab (KEYTRUDA®) ~$25 billion, nivolumab (OPDIVO®) ~$9 billion, cemiplimab (LIBTAYO®) ~$918 million, dostarlimab (JEMPERLI®) ~$175 million. Sales of approved anti-PD-L1 therapies include atezolizumab (TECENTRIQ®) ~$4.2 billion, avelumab (BAVENCIO®) ~$961 million, durvalumab (IMFINZI®) ~$4.2 billion. 2023 sales of approved anti-CTLA-4 therapies include ipilimumab (Yervoy®) ~$2.2 billion.*
7. *FDA Approves Merck's KEYTRUDA® (pembrolizumab) Plus Carboplatin and Paclitaxel as Treatment for Adult Patients With Primary Advanced or Recurrent Endometrial Carcinoma – 17 June 2024 Press Release. Excerpt: "Approval marks the third FDA-approved indication for KEYTRUDA in endometrial carcinoma and the 40th indication for KEYTRUDA in the US"*
8. *Source of sales figures: Bloomberg, Wall Street research reports and Company reports.*
9. *MSD Investor Event at American Society of Clinical Oncology (ASCO) 2024*
10. *Nature Reviews Drug Discovery 22, 264-265 (23 Jan 2023) doi: https://doi.org/10.1038/d41573-023-00017-9.*
11. *Sources of US/EU regulatory approvals for ICIs are FDA/EMA and company reports.*
12. *Rockefeller University, 2011 Nobel Prize in Physiology or Medicine, Ralph M. Steinman*
13. *Ira Mellman; Dendritic Cells: Master Regulators of the Immune Response. Cancer Immunol Res 1 September 2013; 1 (3): 145–149. https://doi.org/10.1158/2326-6066.CIR-13-0102*
14. *Comparison of data is from different clinical trials. Pembrolizumab monotherapy data from publications/EPAR assessment report of KN-042 registrational trial. Given the lack of historical results in negative PD-L1 expressing 1L NSCLC patients who received pembrolizumab monotherapy in KN-042 and other trials, the chart only has data from patients in TACTI-002 with TPS <1%. In 1L NSCLC patients with TPS ≥1%, TACTI-002 has 66% patients with TPS 1-49% and 34% with TPS ≥50%, which compares to KN-042 with ~53% patients with PD-L1 and ~47% patients with PD-L1 TPS ≥50%.*
15. *Immutep press release 14 November 2024 - Immutep's Efti Shows Excellent Survival Data from INSIGHT-003 Trial in Non-Small Cell Lung Cancer*
16. *Shirish Gadgeel et al., Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non–Small-Cell Lung Cancer. JCO 38, 1505-1517(2020). DOI:10.1200/JCO.19.03136*
17. *Immutep press release 3 June 2024 - Immutep Announces Clinical Collaboration with MSD to Evaluate Efti in Combination with KEYTRUDA® (pembrolizumab) in Pivotal Phase III Trial*

** KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.*

IMMUTEP

FAST FACTS

Listings
Australian Securities Exchange (ASX), NASDAQ

Market Capitalisation
A$480.0 million / US$313.2 million (as of 25 November 2024)

Stock Codes
ASX: IMM, NASDAQ: IMMP

Cash & Term Deposits
A$172.3 million / US$119.1 million (as of 30 September 2024)

Issued Capital - Ordinary Shares
1,454,567,846 (as of 25 November 2024)

FOLLOW IMMUTEP'S PROGRESS

Immutep is dedicated to maintaining consistent and clear communications with our investors. In addition to our newsletter, we encourage our shareholders to continue following Immutep's progress in several ways:

- Our website is a good source of information for those in search of details about our company, our management team, and archived information. We encourage everyone to check it out regularly - www.immutep.com.
- Immutep registers all our clinical trials, and the details of participating doctors, on the www.clinicaltrials.gov website, a service of the United States National Institutes of Health. This register is the largest such repository of clinical trial information around the world.
- Immutep's social media channels including X, LinkedIn and Facebook.

Immutep Limited, Level 32, Australia Square, 264 George Street, Sydney NSW 2000

This investor update was authorised for release by Marc Voigt, the CEO of Immutep Limited.

ABN: 90 009 237 889