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Investor Update

Late-Stage Trials & Catalysts Ahead

August 2023

IN THIS ISSUE:

Message from the CEO

Since announcing our late-stage development strategy for eftilagimod alpha (efti) nearly a year ago, I'm really pleased with the substantial progress the team has made on a number of fronts, including broadening our clinical trial pipeline in a de-risked and cost-efficient manner. Our focus remains on advancing efti to marketing approval to bring a promising new cancer immunotherapy to patients and to deliver value for our shareholders.

In this newsletter, we provide an outline of our clinical development strategy and highlight the recent progress we have made. We'll talk about the advantages of the integrated trial design that has been agreed with regulators for our AIPAC-003 trial in metastatic breast cancer, and also discuss TACTI-003 as well as our current planning for our registrational trial in 1st line non-small cell lung cancer.

"Immutep is carving out an accelerated and broad clinical development path for efti, pursuing trials in multiple cancer indications that position the Company, or a partner, to fully exploit efti's potential."

Before moving on, I would like to extend my sincere thanks to our existing and new institutional shareholders including several healthcare-focused funds, and of course our retail shareholders, for their participation in the recent A$80 million offering to support our late-stage and expanding clinical pipeline and extend our cash runway to early 2026.

Clinical Development Strategy and Cost-Efficient Pipeline Expansion

Immutep's late-stage clinical pipeline for efti in combination with anti-PD-1 therapy and/or standard-of-care chemotherapy includes three important cancer indications with unmet medical need:

- **1st line Non-Small Cell Lung Cancer (NSCLC):** Global market will nearly double to $48 billion by 2031*
- **Metastatic Breast Cancer (MBC):** Global market estimated to reach $12.7 billion by 2024*
- **1st line Head & Neck Squamous Cell Carcinoma (HNSCC):** Global market estimated to reach $3.5 billion by 2025*

In addition to the recent initiation of the integrated Phase II/III AIPAC-003 trial in MBC, which includes HR+/HER2-neg/low and triple-negative breast cancer patients, we're actively expanding into additional indications and combination therapies to broaden efti's application and thereby increase its potential value.

Our growing clinical pipeline also includes three capital-efficient investigator-initiated trials, based on interest in efti from key opinion leaders:

- **EFTISARC-NEO:** This investigator-initiated Phase II study will evaluate efti with radiotherapy and an anti-PD-1 therapy (KEYTRUDA®) in up to 40 patients with soft tissue sarcoma, an orphan disease with a very poor prognosis. The study represents the first time efti will be studied in a neoadjuvant, non-metastatic cancer setting. EFTISARC-NEO will be primarily funded by the Polish government and led by Principal Investigators Dr. Katarzyna Kozak and Dr. Paweł Sobczuk at the Maria Skłodowska-Curie National Research Institute of Oncology.

- **INSIGHT-005:** This Phase I study is jointly funded with Merck KGaA, Darmstadt, Germany, and combines efti with Merck KGaA's anti-PD-L1 therapy (BAVENCIO®) to treat up to 30 patients with metastatic urothelial cancer.

- **INSIGHT-003:** This investigator-initiated Phase I trial evaluating efti with anti-PD-1 therapy (KEYTRUDA®) & doublet chemotherapy in 1st line metastatic NSCLC has recently been expanded to 50 patients based on positive early safety and efficacy results including a 67% overall response rate and 91% disease control rate (despite 81% of patients having low or negative PD-L1 expression).

Our clinical development strategy strongly positions Immutep or a potential partner to fully exploit efti's broad potential. Important data updates are expected throughout H2 CY2023 and CY2024 from our ongoing clinical trials.

*Market size estimates in US$ based on data from GlobalData (from May 2023) and Nature Reviews Drug Discovery 22, 264-265 (23 Jan 2023) doi: https://doi.org/10.1038/d41573-023-00017-9.

Multiple Catalysts in 2023

There will be many data-driven catalysts in H2 2023 that should be on our shareholders' radar. As shown below, these include multiple updates from our clinical pipeline including for TACTI-002 and INSIGHT-003, as well as topline results from TACTI-003.

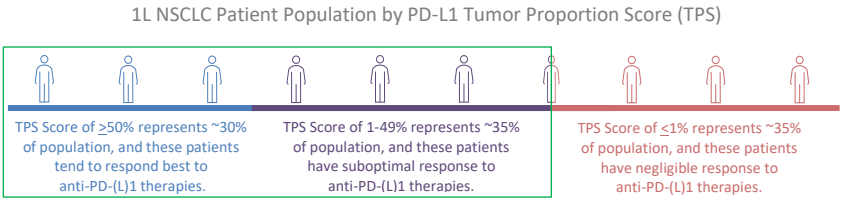
Topline readout from randomised TACTI-003 Phase IIb trial in 1L HNSCC	Data updates from TACTI-002 Phase II trial including Overall Survival	Data updates from triple combination INSIGHT-003 Phase I trial with efti + anti-PD-1 + chemotherapy	Updates on AIPAC-003 Phase II/III trial in MBC
Updates on TACTI-004 Phase III trial planning in 1L NSCLC	Updates on INSIGHT-005 study in urothelial cancer jointly-funded with Merck KGaA, Darmstadt, Germany	IND-enabling studies of IMP761, world's first agonist LAG-3 antibody targeting autoimmune diseases	Updates from partnered programs

Immutep's Late-Stage Trials Addressing Three Important Cancer Indications*

TACTI-004 (**T**wo **ACT**ive **I**mmunotherapies) in 1st line NSCLC

Immutep is prioritising late-stage development efforts to further evaluate efti in **1st line NSCLC** in combination with anti-PD-1 therapy based on compelling data, coupled with the large market opportunity and high unmet need for more durable and tolerable options for patients. Clinical data to date shows efti may be uniquely positioned to address the entire NSCLC patient population, regardless of PD-L1 expression, through both chemo-free immuno-oncology (IO) combinations and IO-IO-chemo triple combinations. Our NSCLC program will be shaped by maturing data from the ongoing TACTI-002 and INSIGHT-003 trials, partnering discussions, along with feedback from regulatory authorities and other stakeholders.

Efti + anti-PD-(L)1 therapy may treat 1L NSCLC patients that have ≥1% PD-L1 TPS (~65% of patient population) with an effective, chemotherapy-free IO-IO regimen →



In Part A of the TACTI-002 Phase II study, efti plus KEYTRUDA® (pembrolizumab) doubled the Overall Response Rate (the number of patients with ≥30% tumour shrinkage) in 1st line NSCLC patients (N=114) as compared to published data with KEYTRUDA® monotherapy. Additionally, efti strengthened responses to KEYTRUDA® across the entire PD-L1 spectrum, including driving clinical benefit for PD-L1 negative patients that typically have negligible response to anti-PD-(L)1 therapies.

Furthermore, the IO-IO combination has achieved an excellent initial median Overall Survival (mOS) benefit of 25.0 months for 1st line NSCLC patients with ≥1% PD-L1 TPS expression (N=58). This initial mOS compares favorably to historical data

**** Among other items, trial designs and timelines are subject to Regulatory Authority interactions and Competent Authority approval***

for patients with ≥1% PD-L1 TPS from registration trials of anti-PD-1 monotherapy (16.4 months mOS) and combinations of anti-PD-1 with chemo (15.8-23.3 months mOS) or with anti-CTLA-4 (17.1 months mOS). See table below.

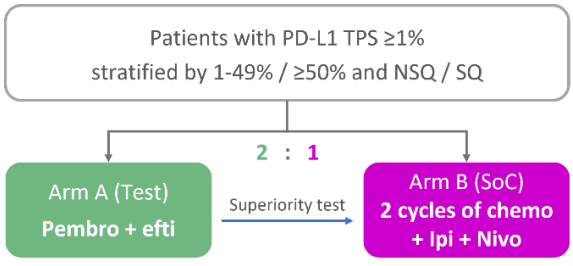
Overall survival of efti + pembrolizumab vs. standard-of-care therapies in 1st line NSCLC, PD-L1 TPS ≥1%

Therapy	Median Overall Survival[2]
Efti + Pembro	25.0 months
Pembro + Doublet Chemo (NSQ)	23.3 months
Pembro + Doublet Chemo (SQ)	18.9 months
Ipi + Nivo[1]	17.1 months
Pembro monotherapy[1]	16.4 months
Ipi + Nivo + limited 2 cycles of Doublet Chemo	15.8 months

Efti + Pembro data: Data cut-off for mOS March 31, 2023. (1) Only in US, not in EU. (2) Arrow lengths are proportional representations. Data for standard-of-care therapies taken from publications of respective registrational trials (e.g. KN-042, KN-407, KN-189, CM-227, CM-9LA) and comparison of data is from different clinical trials.

We are advancing planning for our TACTI-004 Phase III trial to treat 1st line NSCLC patients with ≥1% PD-L1 TPS expression, for which efti + KEYTRUDA® has received FDA Fast Track designation. When planning a Phase III trial one needs to carefully consider the set-up, feasibility, and the potential future label in light of available resources. For Immutep, it is important to address most major markets and be positioned for approval in both the US and EU, which together account for up to 80% of the global market. Accordingly, our current study design is intended to provide a path to achieve this goal.

TACTI-004 will compare efti + KEYTRUDA® against nivolumab + ipilimumab + doublet chemotherapy, an accepted category 1 regimen according to the National Comprehensive Cancer Network® (NCCN), American Society of Clinical Oncology (ASCO), and European Society for Medical Oncology (ESMO) guidelines for 1st line NSCLC patients with ≥1% PD-L1 TPS. While most of the registrational trials for the standard-of-care IO-chemo or IO-IO-chemo combinations listed in the table above were evaluated against chemotherapy alone, TACTI-004 will have a more challenging standard-of-care IO-IO-doublet chemo as the comparator arm. This will provide a clear opportunity to showcase how our chemo-free IO-IO combination using efti can attain superior overall survival, high response rates, strong progression-free survival, extended duration of responses, and potentially better safety as there is no toxic chemotherapy required to achieve these results.



TACTI-004 will be 2:1 randomised and we expect the trial to recruit well driven by high interest in the chemo-free efti + pembro combination, plus many countries having suboptimal standard-of-care (chemo alone) driving interest for the comparator arm too. The trial is expected to begin in H1 of CY2024 and will enroll ~630 patients. The primary objective of the trial will be Overall Survival. A futility analysis is anticipated in H1 of CY2025 after ~225 patients are recruited. If the futility boundary is not hit, we see a good likelihood of TACTI-004 study success based on current data.

We look forward to providing more updates as we move closer to initiating TACTI-004. As noted, among other items, the TACTI-004 trial design and timelines are subject to Regulatory Authority interactions and Competent Authority approval, as well as partnering discussions.

Additionally, efti's unique stimulation of the immune system to fight cancer has shown synergies with both anti-PD-(L)1 therapies and chemotherapy separately. By combining all three modalities in the INSIGHT-003 trial, we hope to drive meaningful responses for 1st line NSCLC patients that have PD-L1 low (TPS 1-49%) or PD-L1 negative (TPS <1%) expression. The early clinical results have been encouraging from both an efficacy and safety perspective, leading to the expansion of the trial to treat 50 patients. We anticipate more results from this promising INSIGHT-003 study during CY2023.

1st line NSCLC is a large patient market with ~1.87 million diagnoses per annum[1]. Sadly, lung cancer is the highest cause of death among all cancers[2]. Only ~20% of 1st line patients respond well to immune checkpoint inhibitor (ICI) monotherapy, and Immutep is focused on improving clinical responses for the many NSCLC patients who develop metastatic disease who are eligible to receive anti-PD-(L)1 therapy.

1 Calculated from Global Cancer Observatory (WHO), 2020 data & American Cancer Society, About Lung Cancer; 2 Informa Pharma Intelligence Report 2018 for US, Japan and EU5

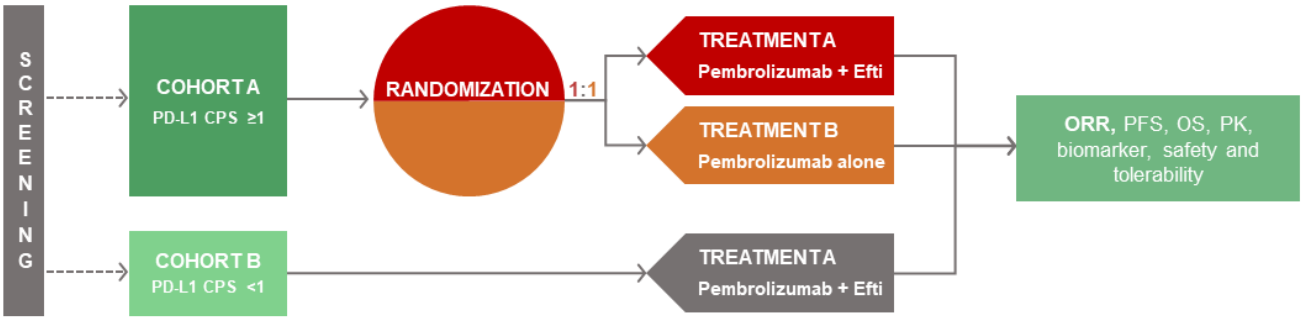
TACTI-003 (**T**wo **ACT**ive **I**mmunotherapies) in 1st line HNSCC

With more than 90% of patients now enrolled, recruitment is progressing well for the randomised TACTI-003 Phase IIb trial pairing efti with KEYTRUDA® (pembrolizumab) to treat **1st line HNSCC,** and we expect to report top line results from the study this year.

The TACTI-003 trial in 1st line HNSCC builds on the positive Phase II clinical results that the IO-IO combination achieved in 2nd line HNSCC as compared to KEYTRUDA® monotherapy in the same patient population, including a doubling of overall response rates, an eight-fold increase in complete responses, and an extended duration of response. These results led to efti receiving Fast Track status in 1st line recurrent or metastatic HNSCC from the United States Food and Drug Administration (FDA), which helps to facilitate the development and expedite the review of drug candidates to treat serious conditions and fill an unmet medical need.

The randomised TACTI-003 Phase IIb trial has two cohorts:

- In Cohort A (est. N=130) efti + KEYTRUDA® is compared to KEYTRUDA® monotherapy for patients whose tumours express PD-L1 (CPS ≥1). We are using CPS 1-19 and CPS ≥20 as stratification factors.
- In Cohort B (est. N=24), patients with negative PD-L1 expression (CPS <1) will receive only efti + KEYTRUDA® as it is well known that these patients do not respond to KEYTRUDA® alone. Therefore, Part B can't be randomized as it would be unethical to provide CPS negative patients with KEYTRUDA® monotherapy. The limited previous clinical research in CPS negative 1st line HNSCC patients with KEYTRUDA® alone delivered an ORR of less than 5%, a clear benchmark for Cohort B.



All in all, the trial has multiple shots on goal: CPS <1, CPS ≥1, CPS 1-19, and CPS ≥20. Additionally, biomarkers will be collected and analysed. Subject to finishing recruitment in the coming months, publication of top line results is planned by the end of CY2023 and a detailed primary analysis according to the protocol is planned for Q1 CY2024.

Immutep has ongoing clinical trial collaboration and supply agreements with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada) for the TACTI-003 and TACTI-002 trials. Since KEYTRUDA's first FDA approval in 2014, it has been approved for a wide range of cancers with its full prescribing list covering over 30 settings. In 2022, KEYTRUDA sales grew to ~US$21 billion, up 22% from ~US$17 billion in 2021. It is expected to become the world's top selling drug.

Efti has shown the ability to safely improve clinical outcomes of anti-PD-(L)1 therapies, such as KEYTRUDA, across multiple clinical trials and various indications including 1st line NSCLC, 2nd line HNSCC, metastatic melanoma, and other advanced solid tumours driving a potential substantial commercial opportunity.

Each year, there are ~900K cases and >400K deaths from HNSCC[1], an aggressive, genetically complex, and difficult to treat cancer.[2] Furthermore, HNSCC is associated with high levels of psychological distress and compromised quality of life.[3] As such, patients with HNSCC are very much in need of improved treatment options. Standard of care therapy for 1st line HNSCC is KEYTRUDA® (pembrolizumab) with chemotherapy for patients with any PD-L1 status, and KEYTRUDA® monotherapy for patients whose tumors express PD-L1 (CPS ≥1)[4,5]

1. Global Cancer Observatory. International Agency for Research on Cancer. World Health Organization. 2. Alsahafi et al. Clinical update on head and neck cancer: molecular biology and ongoing challenges. Cell Death Dis 10, 540 (2019). 3. Johnson et al. Head and neck squamous cell carcinoma. Nat Rev Dis Primers 6, 92 (2020). 4. FDA approval based on KN-048 (ORR, mOS, mDoR data from KN-048 trial). 5. Expert Rev Anticancer Ther. 2021 Dec;21(12):1321-1331. doi: 10.1080/14737140.2021.1996228.

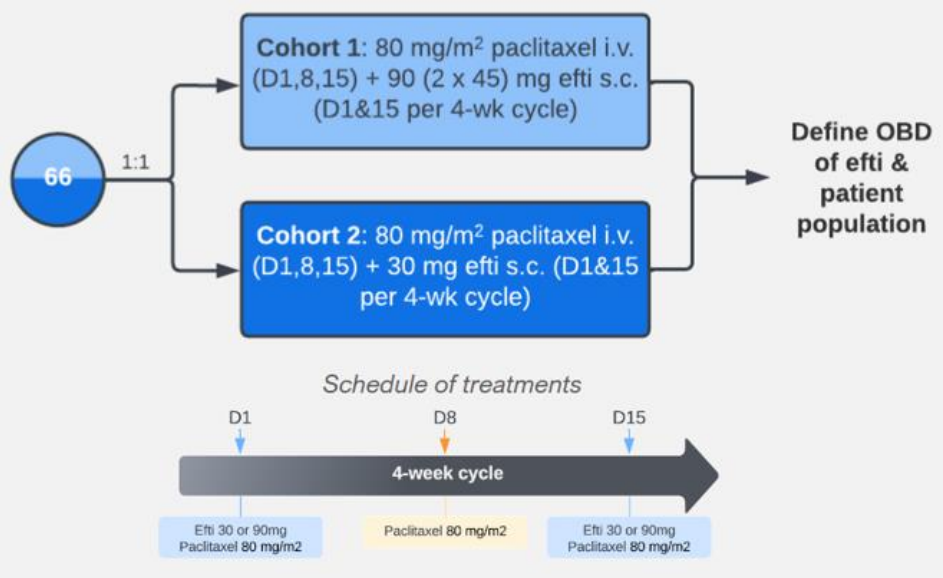
AIPAC-003 (**A**ctive **I**mmunotherapy and **PAC**litaxel) in MBC

In the first quarter of 2023, we initiated AIPAC-003, our integrated Phase II/III trial to evaluate efti in combination with standard-of-care chemotherapy, paclitaxel, for the treatment of **metastatic breast cancer (MBC) patients with HR+/HER2-neg/low and triple negative breast cancer (TNBC).**

As a first-in-class soluble LAG-3 protein targeting a subset of MHC Class II molecules on antigen-presenting cells (APC), efti is uniquely positioned to improve clinical outcomes from standard-of-care chemotherapy. Its activation of APCs (e.g., dendritic cells, monocytes) triggers a broad immune response that includes significant increases in cytotoxic CD8+ T cells that can be armed with chemo-induced tumour antigens to target breast cancer. This synergy was demonstrated by the AIPAC Phase IIb trial's encouraging efficacy and safety, including a +2.9-month median Overall Survival (mOS) improvement, statistically significant mOS improvements between +4.2 to +19.6 months across three pre-specified subgroups, a statistically significant increase in cytotoxic CD8 T cells that correlated with improved Overall Survival, a higher 48% response rate (vs 38% for chemo alone), and a superior Quality of Life preservation.

AIPAC-003 builds upon these encouraging efficacy and safety results with four key adaptations. Unlike the previous AIPAC Phase IIb trial that administered efti and paclitaxel on different days and ceased paclitaxel at six months, AIPAC-003 patients will receive both on the same day and efti + paclitaxel treatment can continue until disease progression. Additionally, we agreed with regulators to expand the trial population to include triple-negative breast cancer patients, and a primary endpoint of overall survival has been selected. The first AIPAC-003 patient was enrolled in May 2023.

Trial design plays a significant role in our clinical development strategy and helps us to maximize the potential of efti in a cost-efficient and risk-balanced approach. When structuring our late-stage trials, Immutep engages with regulatory authorities closely to understand what the requirements would be to consider efti for marketing approval. For our AIPAC-003 trial, we agreed with the FDA on an integrated Phase II/III trial design to help inform a potential Biologics License Application (a request for permission to sell a biologic product in the US). Additionally, the trial design incorporates feedback from the European Medicines Agency (EMA).



The Company and the FDA also agreed to an open-label lead-in component of 6 to 12 patients to evaluate 90mg efti dosing in combination with paclitaxel driven by efti's excellent safety profile, along with the FDA's Project Optimus initiative in oncology. At the time of this newsletter, the first four patients have been receiving their initial 90mg efti injections without experiencing a dose limiting toxicity. After the lead-in component, the Phase II portion of the trial (shown in image above) will be used to the determine the dose (either 30mg or 90mg) and patient population for the randomised Phase III portion of the trial and may influence the dose for the whole efti program.

For Immutep, this integrated Phase II/III trial design offers a prudent, risk balanced approach. It enables us to complete the Phase II portion of the trial within our current budget to detect a strong efficacy signal before we decide to embark on the larger randomized, double-blinded, placebo-controlled Phase III study.

In 2020, there were 2.3 million women diagnosed with breast cancer and 685,000 deaths globally[1].
HR+/HER 2- is the most common type of breast cancer and accounts for ~68% of new cases[2]. TNBC is a clinically aggressive sub-type of breast cancer that accounts for ~15-20% of breast tumors[3]. TNBC is more commonly diagnosed in women younger than 40 years[4].

1. World Health Organization; Breast Cancer Fact Sheet. 2. Cancer Stat Facts: Female Breast Cancer Subtypes - NCI SEER. 3. Front. Mol. Biosci., 19 August 2022, Sec. Molecular Diagnostics and Therapeutics https://doi.org/10.3389/fmolb.2022.903065. 4. The epidemiology of triple-negative breast cancer, including race. Cancer Causes Control. 2009 Sep;20(7):1071-82. doi: 10.1007/s10552-009-9331-1

Board and Management Update

We are pleased to welcome two new members to our team.

At the Board level, Lis Boyce was appointed as Non-Executive Director replacing Lucy Turnbull, who re-joined the Board after the sudden and untimely death of Grant Chamberlain in January 2022. The Board is grateful to Lucy for stepping in under such tragic circumstances and for her boundless energy and valued insights. Ms Boyce is a highly experienced corporate lawyer and currently a partner at Piper Alderman. She has extensive experience in the Life Sciences and Healthcare sectors as well as in capital raisings, strategic collaborations, commercial contracts and mergers and acquisitions. Lis is currently deputy chair of AusBiotech's AusMedtech Advisory Group and a member of AusBiotech's State Committee for NSW.

At the management level, Florian D. Vogl, M.D., Ph.D., has been appointed Chief Medical Officer of Immutep. We are excited to have Florian join our leadership team at this juncture as we progress our late-stage clinical pipeline in oncology and our pre-clinical program in autoimmune diseases. Dr Vogl is a board-certified MD and has over 13 years' experience in the biopharmaceutical industry with extensive clinical development expertise in the field of oncology in Europe and the US through roles at Cellestia Biotech, Rainier Therapeutics, Novartis and Amgen. In addition to his impressive credentials, Dr Vogl brings a wealth of industry knowledge including developing and leading clinical strategy programs from Phase I to Phase IV, as well as broad experience working with regulatory agencies in the US and Europe.

IMMUTEP

FAST FACTS

Listings
Australian Securities Exchange (ASX), NASDAQ

Stock Codes
ASX: IMM, NASDAQ: IMMP

Issued Capital – Ordinary Shares
1,187,306, 209 (as of 17 August 2023)

Market Capitalisation
A$338 million / US$217 million (as of 17 August 2023)

Cash & Term Deposits
A$123.4 million / US$79 million (as of 30 June 2023 from latest Quarterly Activities Report and Appendix 4C)

Upcoming Events

Citi's 2023 18th Annual BioPharma Conference	–	September 6 – 7, 2023
2023 Baird Global Healthcare Conference	–	September 12 – 13, 2023
Bell Potter's Emerging Leaders Conference	–	September 12, 2023
E&P Small Caps Health Care Conference	–	September 13, 2023
2023 Cantor Global Healthcare Conference	–	September 26 – 28, 2023
ESMO Congress 2023	–	October 20 – 24, 2023
Wilsons Drug and Device Healthcare Conference	–	October 25 – 27, 2023
SITC 2023	–	November 1 – 5, 2023
Targets & Cell Types in I-O Europe	–	November 14 – 15, 2023

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 a number of ways:

www.immutep.com

Our website is a treasure trove for those in search of details about our company, our management team, and archived information. We encourage everyone to check it out regularly.

www.clinicaltrials.gov

Immutep registers all of our clinical trials, and the details of enrolling doctors, on the 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.

Our ClinicalTrials.gov ID for our trials are as follows:
- AIPAC-003 trial is NCT05747794
- TACTI-002 trial is NCT03625323
- TACTI-003 trial is NCT04811027

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