immutep
LAG-3 IMMUNOTHERAPY

Investor Update

April 2025

TACTI-004: Changing the Treatment Landscape for Patients with Non-Small Cell Lung Cancer

IN THIS ISSUE

Message from the CEO

I am very pleased to share this investor update. On the 25th of March 2025, Immutep announced the successful dosing of the first patient in our pivotal TACTI-004 Phase III trial in first line non-small cell lung cancer (1L NSCLC), arguably one of our most significant milestones to date. The entire team is excited with this achievement along with our recent regulatory progress with full clearances for the study starting with Australia in December followed by 19 additional countries since. These advancements position us to deliver on our mission to safely provide meaningful clinical benefits for cancer patients in need of more effective, durable therapies.

Immunotherapy's reshaping of the treatment landscape in oncology began in earnest with the approvals of immune checkpoint inhibitors (ICI) such as the anti-PD-1 KEYTRUDA® about a decade ago. We believe the next 10 years will be driven by a new wave of therapies like efti that build upon this initial success. Efti's ability to expand the number of patients that respond to ICIs and extend patients' overall survival through its unique activation of the immune system creates a substantial opportunity. Collectively, ICIs eclipsed $52 billion in sales in 2024 including $29.5 billion from KEYTRUDA, the world's top selling drug.[1,2]

If TACTI-004 is successful in safely driving superior survival for patients, it presents a potential blockbuster commercial opportunity[3] for Immutep as efti will be given alongside KEYTRUDA and chemo, the therapy most often chosen by physicians in advanced/metastatic 1L NSCLC.[4]

"We are very excited to participate in this important Phase III trial. Despite advancements in the treatment landscape for non-small cell lung cancer, there remains a high unmet need for new approaches that can safely extend patients' lives. The anti-cancer immune response driven by efti's unique mechanism of action as an MHC Class II agonist in combination with KEYTRUDA has led to strong efficacy across all PD-L1 levels with favourable safety in multiple lung cancer trials. We hope to see this study confirm the promise of this novel combination to provide patients with a powerful new treatment option."

- ***Dr. Ina Nordman, Calvary Mater Newcastle Hospital***

Targeting Largest 1L NSCLC Patient Population Among Phase III Trials with KEYTRUDA

While ICIs have revolutionised the treatment landscape in NSCLC, as many as 80% of patients do not respond to anti-PD-(L)1 monotherapy. This has driven the biotech and pharma industry to search for therapeutic combinations with anti-PD-(L)1 therapies that can:

Expand patients who respond to PD-(L)1 inhibitors	**Improve clinical outcomes for responders**	**Overcome primary or acquired resistance**

Efti's clinical data to date in combination with KEYTRUDA suggests it can accomplish all three of these objectives for the treatment of advanced/metastatic 1L NSCLC in a safe manner.

On the strength of clinical data in the TACTI-002 and INSIGHT-003 trials, Immutep entered into its most important clinical trial collaboration and supply agreement with MSD (Merck & Co., Inc., Rahway, NJ, USA) for the pivotal TACTI-004 (**T**wo **ACT**ive **I**mmunotherapies) Phase III trial to evaluate efti in combination with KEYTRUDA and chemotherapy as first-line treatment of advanced/metastatic NSCLC regardless of PD-L1 expression, not amenable to EGFR/ALK/ROS1 based therapy.[5]

The TACTI-004 trial design formulated in collaboration with MSD has received positive feedback from the US FDA and other regulatory agencies. Here are key highlights of the trial and collaboration:

- TACTI-004 is a 1:1 randomised, double-blinded, multinational, controlled study that will enrol ~756 NSCLC patients in +150 sites and +25 countries worldwide
- Immutep to conduct trial & retains all commercial rights to efti, and MSD to supply KEYTRUDA (typical ICI drug supply for such a Phase III trial is approximately US$100 million)
- Multiple shots on goal with Progression-Free Survival (PFS) & Overall Survival (OS) as dual primary endpoints and non-squamous & squamous patients regardless of PD-L1 expression
- Prespecified futility boundary anticipated in late 2025 or early 2026 and an interim PFS analysis anticipated year-end 2026 through mid-2027 depending on enrolment and events
- Robust statistics, especially adequate power to provide a good chance of success with a relatively small improvement needed in the hazard ratio

Given the substantial size of the non-small cell lung cancer market with an estimated 2 million cases annually, every 10% of the patient population is meaningful. A key aspect of the TACTI-004 trial design is by enrolling non-squamous and squamous patients regardless of PD-L1 expression (PD-L1 TPS 0-100%), it targets the broadest 1L NSCLC population among multiple Phase III trials that include KEYTRUDA in the treatment arm. As shown in the graphic below, this patient population is 2X to 5X the size of other 1L NSCLC Phase III trials that larger pharmaceutical companies are targeting in collaboration with MSD, including Gilead and Daiichi Sankyo.[6]

	PD-L1 TPS <1	PD-L1 TPS 1-49	PD-L1 TPS ≥50	Non-squamous	Squamous	Total Population
1L NSCLC patient population*	35%	35%	30%	70%	30%	Up to 100%
TACTI-004 (Immutep) Efti + KEYTRUDA + Chemo	✔	✔	✔	✔	✔	**100%**
TROPION-Lung07 (Daiichi Sankyo) DatoDXd + KEYTRUDA	✔	✔	✘	✔	✘	49%
EVOKE-03 (Gilead) Sacituzumab Govitecan + KEYTRUDA	✘	✘	✔	✔	✔	30%
TROPION-Lung08 (Daiichi Sankyo) DatoDXd + KEYTRUDA	✘	✘	✔	✔	✘	21%

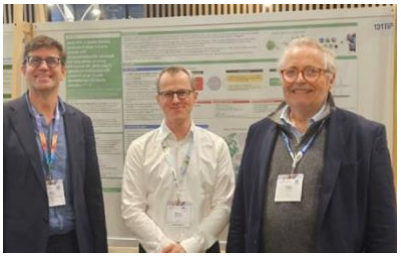
Good Physician Support & Feedback Bolster Expectations Trial will Enrol Well

Efti's key advantages include its excellent efficacy and safety profile with good tolerability. As an agonist, efti has a broad therapeutic window and clinical trials have shown dose-dependent activity starting from below 1 mg up to 30 mg of efti. Importantly, as the dosing increased to the 30 mg level in combination trials with either chemotherapy, PD-1 therapy, or PD-L1 therapy, efti maintained an overall favourable safety profile and its addition typically did not lead to an increase in treatment-related discontinuations as compared to each of those therapies on their own.

Due to the excellent efficacy and strong safety profile of 30 mg efti, and to satisfy FDA's Project Optimus requiring companies to explore dose optimisation before progressing to registration trials,[7] the dosing

level was expanded 3-fold to 90 mg based on FDA request for evaluation in the randomised Phase II portion of the AIPAC-003 trial. We agreed with the FDA at the time on a clear process to determine efti's optimal biological dose (OBD) utilising pre-defined tolerability, pharmacokinetics, pharmacodynamics, safety, and efficacy parameters. As per our ASX announcement regarding first patient dosing in TACTI-004, tolerability issues have been observed with the 90 mg dosing of efti in AIPAC-003 and we have therefore, based on the pre-defined criteria, selected the well-established and clinically active 30 mg dose as the OBD for efti.[8]

We have seen very good support from the investigators taking part in the study in our meetings to date including those held at the European Lung Cancer Congress (ELCC) 2025 on 26 March, where we had the first opportunity to share the trial design via a Trial in Progress poster.



More recently on 10-11 April 2025 in Budapest, Hungary, our team attended and delivered presentations at a fabulous investigator meeting for the TACTI-004 study organised by Fortrea and Scarritt Group, Inc. It has been encouraging to hear consistent feedback that the efficacy and safety data collected thus far from the TACTI-002 and INSIGHT-003 trials is impressive and addresses the unmet medical needs seen by many key opinion leaders (KOLs). Investigators were quite pleased with the study design and the broad inclusions criteria with PD-L1 TPS 0-100%, which will facilitate recruitment.

The shared view of efti as a safe, easy-to-administer, and unique immunotherapy that has shown strong efficacy in 1L NSCLC trials bolsters the prospects for TACTI-004 to enrol well given (1) the control arm is best available standard-of-care, and (2) the treatment arm is the same with the addition of efti.

The ability to drive greater efficacy in a safe manner is the ideal scenario for any drug that can achieve these objectives in tandem. Given the compelling clinical benefits coupled with a favourable safety profile in two separate clinical trials evaluating efti in combination with KEYTRUDA in 1L NSCLC (one with platinum doublet chemotherapy and one without chemotherapy), we continue to believe TACTI-004 has the potential to change the first line treatment paradigm for patients with non-small cell lung cancer.[9]

Markets Overview

The global equity markets for many industries are very difficult and highly volatile, and the biotech industry is no exception with the S&P Biotech Index and Russell 2000 Biotech Index down 16.6% and 20.2% year-to-date, respectively.[10] This performance, one of the weakest among all sectors, is driven by multiple challenges including complex regulatory environments (e.g. FDA staff cuts), elevated interest rates, investor apprehension toward higher-risk investments, among other items. These biotech sector impacts are outside our control and come at a time when we are very optimistic about the fundamentals and outlook of our own business and efti.

While macroeconomic and geopolitical factors are causing challenges for the biotech industry, we are engaging in productive discussions with pharmaceutical executives, industry peers, and portfolio managers who have weathered similar storms, as has our own leadership team. Some are already starting to see this period of high volatility as creating unique opportunities and setting the stage for a strong rebound as the sector has done historically.

One thing is for certain: biotech companies successfully developing drugs that make a meaningful difference in the lives of patients with difficult diseases, such as non-small cell lung cancer, can yield significant, uncorrelated returns for investors. We remain confident in the broad potential of the biotech industry and in particular for Immutep.

Summary

In summary, we are very confident 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 achieved to date across two lung cancer trials evaluating efti with KEYTRUDA in 1L NSCLC patients regardless of PD-L1 expression levels, and particularly as it relates to the compelling data for the OS and PFS dual primary endpoints in the pivotal TACTI-004 trial. Like most large pharma Phase III trials, a reasonable differential between treatment and control arms would lead to the trial's success.

Despite the weakness and volatility in biotech share prices in recent times, valuations can quickly change following positive data from clinical trials and hence we are optimistic about our future prospects as we continue to advance efti towards registration. As we work towards the key milestones in the TACTI-004 study, we have multiple ongoing trials in areas of high unmet need in oncology including INSIGHT-003, TACTI-003, EFTISARC-NEO, and AIPAC-003, as well as our first-in-human Phase I trial of IMP761. This positions us to see a number of catalysts during the course of the year.

Collectively, our clinical strategy strongly positions Immutep or a partner to exploit efti's broad potential. Importantly, we have a very strong cash position and continue to be prudent with our cash management.

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

Footnotes:

1. *Bloomberg & company reports source of 2024 ICI sales; Currency: USD. Anti-PD-1 therapies include pembrolizumab (KEYTRUDA®) ~$29.5B, nivolumab (OPDIVO®) ~$9.3B, cemiplimab (LIBTAYO®) ~$1.2B, dostarlimab (JEMPERLI®) ~$467M. Anti-PD-L1 therapies include atezolizumab ~$4.1B, avelumab, ~$795M, durvalumab ~$4.7B. Sales of approved anti-CTLA-4 therapies include ipilimumab ~$2.5B.*
2. *Bloomberg and company report source of pembrolizumab (KEYTRUDA®) sales of ~$29.5 billion in 2024*
3. *Wall Street estimates for efti in 1L NSCLC range up to $US 3.7 billion on annual basis*
4. *MSD (Merck & Co.) captures between 7 to 8 of every 10 metastatic lung cancer patients as disclosed at MSD Investor Event at American Society of Clinical Oncology (ASCO) 2024*
5. *3 June 2024 - Immutep Announces Clinical Collaboration with MSD to Evaluate Efti in Combination with KEYTRUDA® (pembrolizumab) in Pivotal Phase III Trial*
6. *Sources: Company reports and clinicaltrials.gov. Patient population estimates by PD-L1 expression based on market research and enrolment across 1L NSCLC clinical trials.*
7. *FDA Project Optimus - https://www.fda.gov/about-fda/oncology-center-excellence/project-optimus*
8. *25 March 2025 - First Patient Dosed in Immutep's TACTI-004 Phase III Trial in First Line Non-Small Cell Lung Cancer*
9. *Immutep's Efti in Combination with KEYTRUDA® Generates Excellent Overall Survival Benefit in Patients with Metastatic Non-Small Cell Lung Cancer - October 2023; Immutep's Efti Shows Excellent Survival Data from INSIGHT-003 Trial in Non-Small Cell Lung Cancer, - November 2024*
10. *Bloomberg source of index returns as of 16 April 2025*

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

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FAST FACTS

Listings
Australian Securities Exchange (ASX), NASDAQ

Market Capitalisation
A$357.8 million / US$223.4 million
(as of 22 April 2025)

Stock Codes
ASX: IMM, NASDAQ: IMMP

Cash & Term Deposits
A$159.3 million / US$99 million
(as of 31 December 2024)

Issued Capital – Ordinary Shares
1,460,389,575 (as of 22 April 2025)

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.

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