immutep
Empowering the Immune System

Investor Update

November 2026

Understanding the Path Forward

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A Message from CEO Marc Voigt

The discontinuation of TACTI-004 in March 2026 was deeply disappointing for patients, investigators and shareholders. We committed to examining the unexpected result carefully through a comprehensive root cause analysis (RCA). That work has two aims: to understand what occurred in TACTI-004, and to determine how the findings should shape efti's future development.

While the RCA is ongoing, the findings to date have already informed a more focused path forward for efti. That path is also grounded in the substantial body of clinical data from earlier studies, which continues to provide evidence of efti's potential in oncology. A further discussion of our current findings from the RCA is provided in the TACTI-004 Root Cause Analysis and Shareholder Questions sections below.

The outcome of the RCA is anticipated to be provided at the Company's upcoming Annual General Meeting on 27 November 2026.

All batches of efti used in TACTI-004 met their predefined release specifications and comparability requirements. However, as we reported in September, the RCA has identified subtle structural differences between the efti used in TACTI-004 manufactured at 2,000 L scale and the material used in earlier clinical studies manufactured at 200 L scale, including in the glycan structures attached to the fusion protein. We consider these differences potentially relevant given the markedly different immune activation profile observed in TACTI-004 compared to previous studies and the unexpected outcome of the trial.

We have contracted the manufacture of a new 200 L batch of efti and considered which clinical development opportunities are most compelling. Our strategy now aims at a focused set of clinical targets, subject to final decisions on strategy and trial design, as well as regulatory interactions, manufacturing timelines, partnering and resources.

Specifically, we are prioritising potential registration-directed development of efti in head and neck squamous cell carcinoma (HNSCC) with CPS <1 and neoadjuvant soft tissue sarcoma (STS). These indications are attractive opportunities for efti, and they are also supported by FDA Fast Track and Orphan Drug Designations, respectively.

At the same time, we are progressing IMP761 as a separate clinical-stage opportunity supported by its own manufacturing process and development pathway in autoimmune disease. IMP761 has

delivered very encouraging results in the Phase I study to date which, we believe, support continued clinical development. Late-breaking data presented at ACR Convergence 2026 on 10 November showed statistically significant, exposure-dependent inhibition of T-cell-driven immune responses in healthy volunteers. As a first-in-class LAG-3 agonist antibody, IMP761 has potential across a range of autoimmune diseases and could ultimately be developed both as a monotherapy and in combination with other therapies.

Finally, I sincerely acknowledge the disappointment and financial impact that the TACTI-004 outcome and subsequent share price reaction have had on our shareholders. We recognise that this has been a significant setback, particularly for those who have supported Immutep over many years. At the same time, we are grateful for the many encouraging and supportive messages we continue to receive from shareholders and partners who recognise the potential of our science and pipeline. We do not take this trust and support for granted. Our responsibility now is to incorporate the learnings from the RCA into our strategy and to execute it with discipline and transparency. We remain committed to rebuilding confidence through our actions and progress.

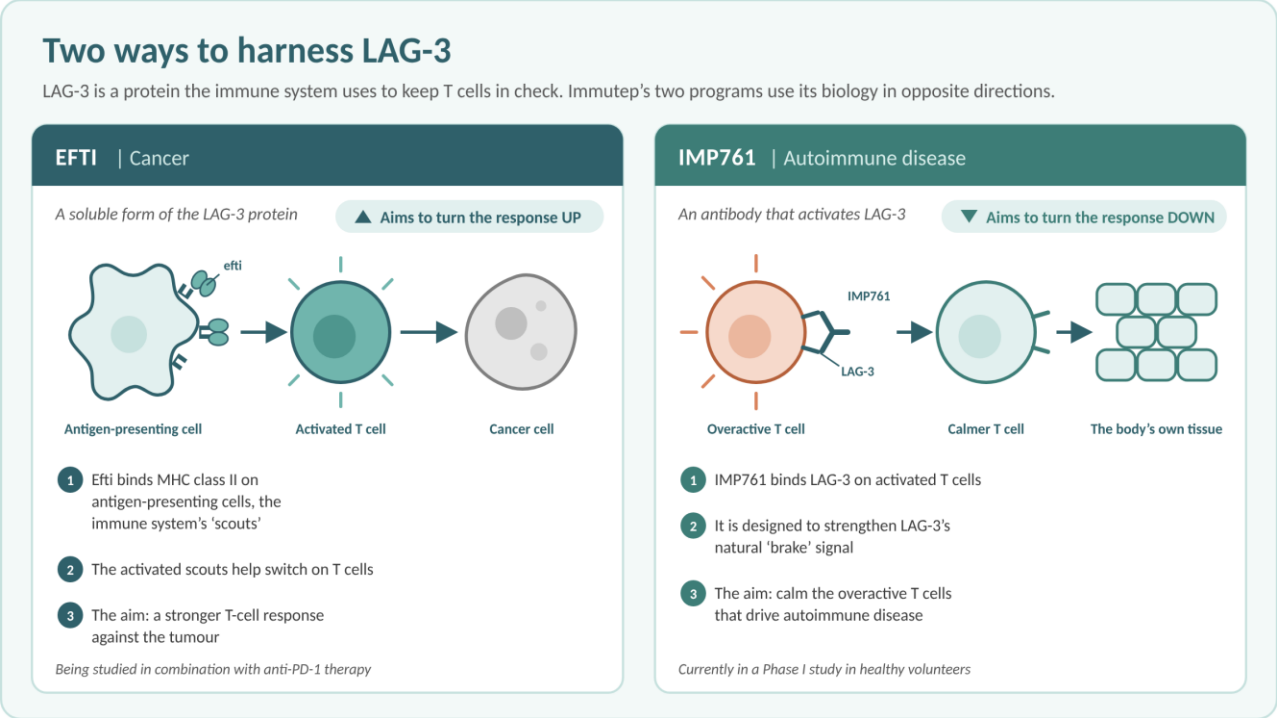
Marc Voigt | Chief Executive Officer

Recent Highlights

Over the past few weeks, Immutep has announced new data from both of its clinical programs.

- **First survival data from EFTISARC-NEO in soft tissue sarcoma.** The abstract released for the CTOS 2026 Annual Meeting reported a 12-month disease-free survival rate of 81.1% in 38 evaluable patients after a median follow-up of 19.1 months. The disease-free survival rate is the proportion of patients who remained alive without their cancer returning. At 12 months, 94.1% of patients had no return of cancer at the original site (local recurrence-free survival) and 86.2% had no spread of cancer to other parts of the body (distant metastasis-free survival). These are preliminary results for secondary endpoints of an investigator-initiated, open-label Phase II study (data cut-off 30 April 2026), and follow-up is ongoing.
- **Quality of life remained stable during EFTISARC-NEO treatment.** Data presented at the ESMO Congress 2026 in Madrid in October showed no statistically significant deterioration on any measured quality of life scale during treatment, and statistically significant improvements after surgery, including in the overall summary score and patient-reported fatigue.
- **New IMP761 data at ACR Convergence 2026.** Immutep's late-breaking poster, presented in Orlando on 10 November, showed that a single infusion of IMP761 produced statistically significant, exposure-dependent inhibition of T-cell-driven immune responses in healthy volunteers, with greater effects seen at higher drug exposure. IMP761 was well tolerated across all seven dose levels tested. Results from the multiple ascending dose part of the study (which tests repeated doses at increasing levels) are anticipated in H1 CY2027.

An Overview of Immutep's Lead Assets



Eftilagimod alfa (efti): activating the immune system against cancer

Efti is an investigational soluble LAG-3 protein designed to activate antigen-presenting cells (immune cells that help direct the rest of the immune system to attack a tumour) and strengthen the body's immune response against cancer. Immutep has evaluated efti in combination with immune checkpoint inhibitors and other therapies. Following TACTI-004, Immutep is concentrating development planning on indications with encouraging patient data, high unmet medical need, limited competition and a supportive regulatory pathway.

IMP761: reducing unwanted immune activation

IMP761 is an investigational LAG-3 agonist antibody (an antibody that switches on LAG-3, one of the immune system's natural 'brakes') intended to dampen unwanted T-cell activation in autoimmune disease. Unlike efti, which aims to stimulate immunity in oncology, IMP761 is designed to suppress harmful immune responses. While Phase I findings in healthy volunteers support further investigation, they do not yet establish clinical efficacy in patients with autoimmune disease. Immutep plans further clinical evaluation in autoimmune diseases driven by T-cell-mediated inflammation, such as rheumatoid arthritis or type 1 diabetes. Immutep's Corporate Presentation released on 20 August 2026 cites GlobalData market estimates for three of the larger diseases in which IMP761 may have application: rheumatoid arthritis (approximately US$29.6 billion across eight major markets in 2029), type 1 diabetes (approximately US$9.9 billion across seven major markets in 2033) and multiple sclerosis (approximately US$32.9 billion across seven major markets in 2028).

These figures estimate the total size of each treatment market. They are not forecasts of IMP761 sales, and IMP761 remains at an early stage of development.

Immutep will treat these two assets as co-priorities, with development pathways and resource allocation guided by emerging data and disciplined decision-making.

Immutep's strengths extend beyond its two lead candidates, efti and IMP761. The Company has built a broad foundation in LAG-3 biology and immunotherapy, supported by extensive intellectual property, longstanding industry partnerships, an experienced team, and deep development expertise. Together with a cash position of A$48.50 million (cash and term deposits) at 30 September 2026, which is expected to fund the Company well into H1 CY2028, these assets and capabilities provide Immutep with multiple opportunities to create value as the Company advances its focused development strategy.

A New Focus for the Development of Efti

First-line head and neck squamous cell carcinoma (HNSCC), PD-L1 CPS <1

In the 31 evaluable patients in Part B of TACTI-003 (HNSCC, CPS <1), efti plus pembrolizumab achieved a 35.5% objective response rate (the proportion of patients whose tumours shrank by a predefined amount) (data cut-off 31 March 2025).

These results support further investigation in a well-defined patient population of meaningful size, with high unmet medical need and relatively few treatment options. Efti has received FDA Fast Track designation in first-line HNSCC, and Immutep has received constructive FDA feedback for further development of a chemotherapy-free treatment in patients with CPS <1.

Final overall survival data will be presented at the ESMO Immuno-Oncology & Advanced Therapies Congress in London on 14 December 2026.

Soft tissue sarcoma (STS): treatment before surgery

Patients with medium- to high-risk, resectable soft tissue sarcoma (STS) face a significant risk of disease recurrence, despite surgery and radiotherapy. There are currently no immunotherapies approved for use in the neoadjuvant setting (before surgery) in STS, highlighting the opportunity for new treatment approaches. The investigator-initiated EFTISARC-NEO Phase II study is currently evaluating efti in combination with pembrolizumab and radiotherapy before surgery. The study met its primary endpoint, achieving a median tumour hyalinisation and fibrosis rate of 51.5% (a measure, taken at surgery, of how much of the tumour had been replaced by scar-like tissue, a sign of treatment effect) in 38 evaluable patients, exceeding the prespecified target of 35%. These encouraging findings support further investigation of whether adding efti-based immunotherapy to established treatment approaches could improve outcomes for patients with resectable STS. The first survival data from EFTISARC-NEO were released on 11 November (see Recent Highlights). Further analyses will be presented at the CTOS 2026 Annual Meeting in Seoul on 19 November 2026 and will be the subject of a separate announcement.

In April 2026, the FDA granted efti Orphan Drug Designation for the treatment of STS. This designation provides potential regulatory and development incentives, including seven years of US market exclusivity if the product is subsequently approved for the designated indication.

Immutep has disclosed a target of H2 CY2027 for starting future efti studies, subject to clinical design, regulatory interactions, manufacturing, partnering and resources.

TACTI-004 Root Cause Analysis: What is Known

Efti is a fusion protein produced by living cells. Proteins produced in this way undergo post-translational modifications (PTMs), such as the attachment of glycan (sugar) structures via glycosylation. These PTMs can generate subtle variations in the manufactured product, even under industry standard quality controls. Following the unexpected outcome of TACTI-004, Immutep initiated a comprehensive root cause analysis (RCA) covering clinical, operational, pharmacological and manufacturing factors.

An important finding emerged from the immune-monitoring data. A pooled analysis of 592 patients across five earlier clinical studies (TACTI-mel, TACTI-002, TACTI-003, AIPAC and AIPAC-003), presented at ASCO 2026, showed that treatment with efti plus standard-of-care (SOC) was associated with a significant increase in circulating absolute lymphocyte count (ALC), the number of lymphocytes (a type of white blood cell central to immune responses) in the blood, an effect not observed with SOC alone. Notably, in the efti plus SOC group, ALC responders experienced significantly improved overall survival compared with ALC non-responders, whereas no corresponding association between ALC response and overall survival was observed in patients receiving SOC alone. These findings are consistent with efti's established mechanism of action.

In contrast, patients treated with efti in TACTI-004 showed a markedly different immune activation profile, including lower circulating lymphocyte and monocyte counts compared with previous efti studies. This unexpected difference provided an important reason to investigate whether the efti used in TACTI-004 differed from the material used in previous studies.

The ongoing RCA has since identified subtle structural differences between efti manufactured at 2,000 L scale for TACTI-004 and the 200 L material used in earlier clinical studies. These include a difference in glycan structure. These findings may be relevant to understanding the unusual immune-monitoring results and the unexpected clinical outcome.

For clarity, the Company notes that all of the batches used in TACTI-004 met their predefined acceptance criteria and applicable comparability requirements. In particular, the required comparability data were submitted to regulators. While subtle structural differences between 2,000 L and 200 L scale material have been detected through additional, more sensitive analyses undertaken after the unexpected clinical result, this does not, on its own, mean that a batch failed quality controls or that an earlier manufacturing decision was improper.

Shareholder Questions: RCA, Glycans and Manufacturing

Q: What exactly is a glycan, and why does it matter?

A: A glycan is a sugar structure attached to a protein at a specific molecular site. Although these sugar structures are small, they can play an important role in how a biologic medicine behaves, including its biological activity, interactions with immune cells, how quickly it is absorbed and how long it remains in the body. The significance of glycosylation is well established across the biopharmaceutical industry. Published work on the approved antibody trastuzumab illustrates this: across many commercial batches, a gradual drift in two glycan features was detected using advanced analytical methods and was accompanied by similar trends in laboratory measures of the antibody's ability to recruit immune cells to kill cancer cells.

Another example is erythropoietin-based medicines used to treat anaemia. Differences in glycosylation can influence how quickly these proteins are cleared from the body and therefore how long they remain active. These examples demonstrate that even relatively subtle structural features of biologic medicines can have meaningful biological consequences.

Q: Does a difference in glycan structure mean the 2,000 L material should have been identified as defective in the manufacturing process?

A: The relevant batches met their acceptance limits and applicable comparability requirements. Regulatory-grade biologics are assessed against predefined specifications, using validated analytical methods and the scientific knowledge available at the stage of development. More sensitive retrospective testing can identify differences that routine release methods did not previously reveal, or that were masked by the normal variability of those methods. Because glycan features can influence biological activity, they are generally monitored as quality attributes. A difference in such a feature is not, however, evidence in itself that a batch was defective.

Q: Was moving from 200 L to 2,000 L a mistake?

A: Scaling up biologics manufacturing is an established, highly regulated activity. Scale changes require process controls, analytical characterisation and appropriate comparability assessments.

The analytical work performed at that stage of efti's clinical development was in line with regulatory expectations and established industry practice for biologics, drawing on precedent from many monoclonal antibodies and fusion proteins to define a robust process designed to deliver a product with reproducible properties. Detailed structural characterisation of glycans requires extensive mass spectrometry analysis. This level of analysis is mainly used for extended product characterisation, rather than for routine manufacturing control and release of monoclonal antibodies and fusion proteins like efti.

The method used to test efti batches routinely at release was consistent with industry practice. It checked for the presence of glycans, but not their location on the protein or their detailed structures. The RCA has now identified subtle differences in the structures of glycans between certain efti

batches and scales. Immutep intends to use these glycan findings to help ensure future efti material closely matches the 200 L material used in earlier studies. The unexpected trial outcome warranted further investigation, but the RCA findings do not demonstrate that the decision to scale up was a mistake.

Q: Why manufacture another 200 L batch?

A: The 200 L process was used to manufacture the efti used in several earlier studies that generated encouraging data. Preparing new material at that scale is a prudent way to preserve development options while the RCA continues and future study plans are refined. The 200 L process would be sufficient in scale to develop efti for smaller indications such as HNSCC CPS <1 and STS. Larger scale, such as 2,000 L, would be required to support other indications with larger patient populations. A future optimised process scale-up program remains a potential additional step.

Q: How tightly regulated is the manufacture of a biologic and subsequent introduction into a clinical trial, for example in the EU?

A: Manufacturing begins with a controlled cell bank and defined process under Good Manufacturing Practice (GMP). The product undergoes extensive testing for identity, purity, potency, safety, stability and relevant structural attributes such as glycosylation. Changes in process or scale require documented change control, comparability assessment and scientific justification and may require an amendment to the clinical trial application. For an EU trial, the Sponsor submits the protocol and investigational medicinal product quality documentation through the Clinical Trials Information System (CTIS) under the EU Clinical Trials Regulation. The regulatory authorities and ethics committees assess the application. Separately, the investigational product must meet applicable GMP and import requirements, with a Qualified Person (QP) certification before each batch is released for clinical use. These are complementary safeguards, not substitutes for one another.

Q: Does this regulatory framework mean that something went wrong previously?

A: These controls are standard for biologics development and apply regardless of whether a company has experienced an unexpected trial outcome. GMP compliance, comparability assessment, regulatory authority and ethics review, and QP certification are designed to manage quality and participant safety. They cannot guarantee that a treatment will succeed in a clinical study. The RCA is a separate scientific investigation into the unexpected TACTI-004 result.

November and December Calendar

Dates to Follow

19 November 2026	CTOS 2026 Annual Meeting, Seoul: EFTISARC-NEO poster discussion on disease-free survival.
27 November 2026, 11:30 a.m. AEDT	Immutep Annual General Meeting: RCA outcome anticipated.
14–16 December 2026	ESMO Immuno-Oncology & Advanced Therapies Congress, London: TACTI-003 (Part B) final median overall survival data.

The AGM will be an opportunity to discuss the scientific findings, the manufacturing strategy, and how Immutep is balancing its oncology and autoimmune development priorities. This newsletter is intended to provide background for that discussion, not to pre-empt any new announcement.

Important Notice and Forward-Looking Statements

This newsletter is for general shareholder information and is not financial product advice, an offer of securities or a substitute for Immutep's ASX announcements and SEC filings. Statements regarding the RCA, clinical data, manufacturing, trial plans, regulatory interactions and future milestones involve uncertainties and assumptions; actual outcomes may differ materially. No definitive causal explanation for the TACTI-004 outcome has been established. Efti and IMP761 are investigational and have not been approved for use by any regulator. Early-stage and single-arm findings are not proof of clinical efficacy or comparative benefit. Shareholders should refer to Immutep's most recent annual and quarterly reports and risk disclosures. All scientific conference data remain subject to applicable embargoes and authorised public disclosure. Interim and preliminary results, including the EFTISARC-NEO survival data, may change as data mature. Cash runway expectations are based on current plans and assumptions and may change.

FOLLOW IMMUTEP'S PROGRESS

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

- 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.immutep.com.
- Immutep registers all of its clinical trials, and the details of enrolling 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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The investor update was authorised for release by the Board of Immutep Limited.