Translational Data and Significant Pathologic Response Rates from EFTISARC-NEO Phase II Highlighted in Oral Presentation at CTOS 2025

- Novel combination with neoadjuvant eftilagimod alfa (efti) achieves significant 51.5% tumour hyalinization/fibrosis across multiple soft tissue sarcoma subtypes including rare and highly aggressive tumours with poor prognosis
- Early translational data show a strong immune system activation inline with efti's mode of action with statistically-significant increases in multiple cytokines and chemokines
- High levels of key immune proteins in EFTISARC-NEO including interferon-gamma (IFN-γ) correlate with pathologic responses indicating a significant destruction/alteration of tumour tissue following treatment, which is generally associated with better outcomes for patients and potentially improved survival rates

SYDNEY, AUSTRALIA – November 13, 2025 – Immutep Limited (ASX: IMM; NASDAQ: IMMP) ("Immutep" or "the Company"), a late-stage immunotherapy company targeting cancer and autoimmune diseases, today announces positive data from the EFTISARC-NEO trial that were detailed in an oral presentation by Paweł Sobczuk, M.D., Ph.D., Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland, at the Connective Tissue Oncology Society (CTOS) 2025 Annual Meeting held in Boca Raton, Florida.

The investigator-initiated Phase II study evaluating eftilagimod alfa (efti) with radiotherapy plus KEYTRUDA® (pembrolizumab) in the neoadjuvant setting for resectable soft tissue sarcoma (STS) significantly exceeded the study's prespecified level of pathologic response rates. In the evaluable patient population (N=38), the novel combination with efti reached a median 51.5% tumour hyalinization/fibrosis ($p<0.001$), meeting the study's primary endpoint.[1]

These promising results were achieved in patients with ten different STS subtypes including rare and/or highly aggressive tumours with poor prognosis such as myxofibrosarcoma (N=16), undifferentiated pleomorphic sarcoma (N=10) and malignant peripheral nerve sheath tumor (N=2).

Early translational data from the initial twenty patients who underwent surgery in the trial show a strong immune system activation in line with efti's mode of action, with statistically significant increases in the expression of key cytokines and chemokines in peripheral blood — specifically CXCL9, CXCL10, IL-23, and IFN-γ.

Immune Response Biomarkers *(fold change from week 1 through pre-surgery)*

Serum Biomarker	Fold change (p-value)
C-X-C motif chemokine ligand 9 (CXCL9)	2.5x ($p<0.01$)
C-X-C motif chemokine ligand 10 (CXCL10)	1.8x ($p<0.0001$)
Interleukin-23 (IL-23)	2.2x ($p<0.05$)
Interferon-gamma (IFN-γ)	2.5x ($p<0.05$)

The increase on treatment of immune response biomarkers like IFN-gamma correlated with pathologic responses in this study, meaning patients with a biomarker increase during treatment also had a higher probability of a good clinical response at surgery.

The promising tumour hylanization/fibrosis rate achieved (over 3X greater than standard-of-care radiotherapy based on historical data)[1] may hold significance in terms of future outcomes as it serves as an early surrogate endpoint correlated with enhanced overall survival and recurrence-free survival in STS patients.[2,3] Disease-free survival and overall survival data are immature at this stage and will be presented in the future. Further correlative translational studies are also ongoing.

Dr. Paweł Sobczuk, one of the trial's principal investigators, stated: "We are excited to share these strong results in resectable soft tissue sarcoma, a challenging indication with a high unmet medical need. This level of efficacy, observed across ten different STS subtypes including rare, highly aggressive tumours with poor prognosis, further supports the hypothesis that efti's distinctive activation of antigen-presenting cells—and consequent induction of both adaptive and innate immunity—plays a key role in driving a coordinated immune response to fight cancer. This novel combination with neoadjuvant efti warrants further investigation in registrational settings."

"Our team was delighted to have recently been awarded the distinguished Golden Scalpel Award (Złoty Skalpel)* for EFTISARC-NEO. This honour is reserved for projects that demonstrate exceptional innovation and impact in medical research and clinical practice," added Dr. Sobczuk.

Dr. Frédéric Triebel, CSO of Immutep, said: "We are pleased to see a confirmation of earlier promising data on now 38 patients in this difficult-to-treat cancer. The prolonged increase in serum immune response biomarkers, observed two weeks after efti subcutaneous injection, is indicative of a robust adaptive and innate immune response. This enhanced immune activity is crucial because it means the body's own defences are being mobilised to target and destroy cancer cells more effectively, further supporting the positive impact of the observed pathologic responses. The recent results suggest that efti may have potential applications beyond advanced or metastatic cancer, extending into earlier-stage disease."

As neoadjuvant immunotherapy becomes more established in the treatment of early-stage cancers, the findings from EFTISARC-NEO highlight the possibility for efti to be used in patients who have a lower tumor burden at diagnosis. This could expand the range of patients who might benefit from efti, potentially increasing its role in the treatment landscape for cancers that are still localized and resectable.

STS is an orphan disease with high unmet medical need and a poor prognosis for patients. The incidence of STS varies in different regions globally. In the United States, the number of new STS cases in 2025 is estimated to be ~13,520 with ~5,420 deaths, according to the American Cancer Society.[4]

For more information on EFTISARC-NEO, visit clinicaltrials.gov (NCT06128863). The CTOS 2025 oral presentation slides can be found on the Posters & Publications page of Immutep's website.

***About the Golden Scalpel Award in Poland**

The Golden Scalpel Award in Poland is recognized as a benchmark of excellence within the medical community. It is presented by independent experts to initiatives that set new standards in advancing healthcare. This year, EFTISARC NEO was the only oncology project to receive this accolade, underscoring its leadership and breakthrough potential in cancer treatment.

About Eftilagimod Alfa (Efti)

Efti is a novel immunotherapy that directly activates antigen-presenting cells or APCs (e.g. dendritic cells, monocytes) via the MHC Class II pathway to fight cancer. As an MHC Class II agonist, its activation of APCs engages the adaptive and innate immune system to initiate a broad anti-cancer immune response. This includes priming and activating cytotoxic T cells as well as generating important co-stimulatory signals & cytokines that further boost the immune system's ability to combat cancer.

Efti is under evaluation for a variety of solid tumours including non-small cell lung cancer (NSCLC) in a pivotal Phase III trial called TACTI-004 (KEYNOTE-F91), as well as head and neck squamous cell carcinoma (HNSCC), soft tissue sarcoma, and breast cancer. Its favourable safety profile enables various combinations like with anti-PD-[L]1 immunotherapy, radiotherapy, and/or chemotherapy. Efti has received Fast Track designation in first line HNSCC and in first line NSCLC from the United States Food and Drug Administration (FDA).

About Immutep

Immutep is a late-stage biotechnology company developing novel immunotherapies for cancer and autoimmune disease. The Company is a pioneer in the understanding and advancement of therapeutics related to Lymphocyte Activation Gene-3 (LAG-3), and its diversified product portfolio harnesses LAG-3's ability to stimulate or suppress the immune response. Immutep is dedicated to leveraging its expertise to bring innovative treatment options to patients in need and to maximise value for shareholders. For more information, please visit www.immutep.com.

1. ESMO Congress 2025 Proffered Paper presentation, "EFTISARC-NEO: A phase II study of neoadjuvant eftilagimod alpha, pembrolizumab and radiotherapy in patients with resectable soft tissue sarcoma".
2. Schaefer IM et al. Histologic Appearance After Preoperative Radiation Therapy for Soft Tissue Sarcoma: Assessment of the European Organization for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group Response Score. Int J Radiat Oncol Biol Phys. 2017 Jun 1;98(2):375-383. doi: 10.1016/j.ijrobp.2017.02.087. Epub 2017 Feb 24. PMID: 28463157.
3. Rao SR et al. Extent of tumor fibrosis/hyalinization and infarction following neoadjuvant radiation therapy is associated with improved survival in patients with soft-tissue sarcoma. Cancer Med. 2022 Jan;11(1):194-206. doi: 10.1002/cam4.4428. Epub 2021 Nov 27. PMID: 34837341; PMCID: PMC8704179.
4. American Cancer Society statistics: https://www.cancer.org/cancer/types/soft-tissue-sarcoma/about/key-statistics.html

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