

# A Global Leader in LAG-3 Therapeutics in Oncology and Autoimmune Disease

**AGM Presentation – November 2022** 

(ASX: IMM, NASDAQ: IMMP)

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## Immutep Overview



## Pioneering LAG-3 Portfolio in Oncology & Autoimmune Disease

Immutep is a pure-play LAG-3 clinical-stage company with four product candidates that address significant market opportunities in oncology & autoimmune disease



#### **Collaborations with Industry Leaders**













#### **Compelling Clinical Data**

Clinical trials of lead candidate eftilagimod alpha (efti) with immunotherapy & chemotherapy have shown compelling results in NSCLC, HNSCC, HR+/HER2-BC, melanoma and other solid tumors







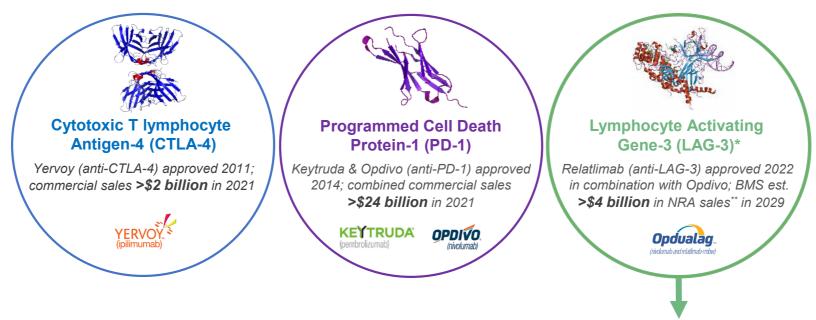


Supported by strong clinical results and increasing trial momentum, Immutep has continued to forge its leadership role in the recently validated LAG-3 landscape

## LAG-3: Approved Checkpoint with Unique Characteristics



Immune system's role in controlling cancer has led to regulatory approval of immunotherapies targeting CTLA-4, PD-1, and now LAG-3 checkpoints



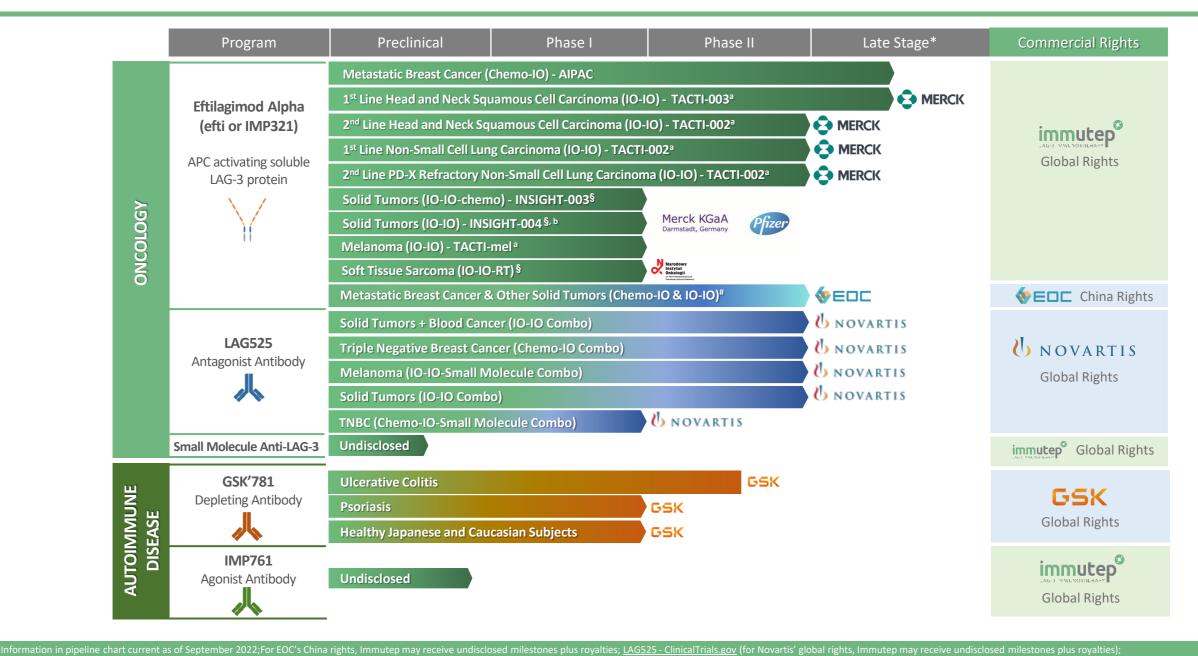
LAG-3 is unique in that its inhibition on T cells & activation of dendritic cells engages the adaptive & innate immune systems against cancer offering significant potential to: (1) improve responses to standard-of-care immunotherapy & chemotherapy, (2) limit emergence of resistance, (3) offer chemotherapy-free options in select indications.



## Immutep Pipeline Update

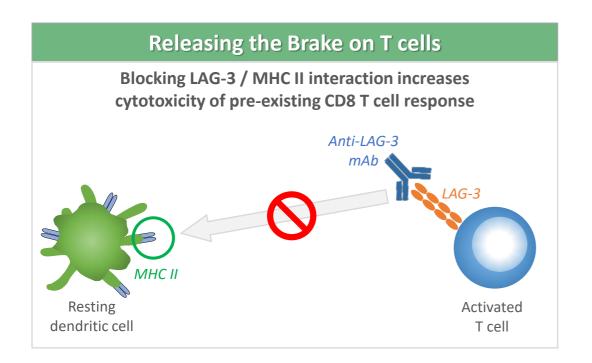
## Immutep LAG-3 Pipeline





## Multiple Companies Targeting LAG-3 Inhibition







- Immutep designed the first anti-LAG-3 antibody and licensed it to CoStim Pharmaceuticals in 2012, which was acquired by Novartis in 2014
- Novartis' anti-LAG-3 mAb, LAG525, activates effector T cells & inhibits regulatory T cells (removing two brakes on the immune system to respond to and kill cancer cells) and has been tested in multiple clinical trials combined with spartalizumab (anti-PD-1) and chemotherapy\*\*
- IP estate for LAG525 continues to strengthen with patent grants in key markets including US, Europe, Japan and China
- Today, Immutep is pioneering a small molecule, oral anti-LAG-3 approach that may offer convenience at fraction of cost of other approaches

## Efti: First-in-Class Positioning in LAG-3 Oncology Landscape



# Eftilagimod alpha (Efti) LAG-3 Human IqG1

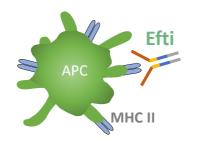
Immutep's proprietary soluble LAG-3Ig clinical candidate is a first-in-class antigenpresenting cell (APC) agonist via MHC II that capitalizes on LAG-3's unique characteristics

## Pushing the Accelerator on the Immune System

APC activation with Efti Anti-tum

Anti-tumor immune cell activation









T-cells









NK Cells

Monocytes

IFN-y

CXCL10

#### Efti, a soluble LAG-3 protein, acts as a key to unlock broad activation of the immune system

- Capitalizes on LAG-3's unique ability to drive adaptive & innate immune systems against cancer
- Has high affinity for a subset of MHC II ligand on APCs
- Its activation of APCs drives broad stimulation of multiple anti-tumor cells, as well as a significant increase in IFN-y and CXCL10 serum biomarkers for systemic TH1 response

#### **Compelling pairing capabilities**

- Excellent safety profile drives high suitability for combination approaches
- Synergistic activity & encouraging clinical results with multiple agents including anti-PD-1, anti-PD-L1, and chemotherapy
- Enhances clinical activity of anti-PD-1 across PD-L1 status, including low & negative PD-L1 tumors

## LAG-3 Leadership



Immutep has more LAG-3 product candidates in development than any other biotech or big pharmaceutical company



#### **LAG-3 Pioneer**

French immunologist Prof Frédéric Triebel, Immutep Executive Director, CMO & CSO, discovered the LAG-3 gene and founded Immutep S.A.

#### Efti data selected for SITC 2022 Press Conference

Immutep's late-breaking abstract for 1<sup>st</sup> line non-small cell lung cancer patients from Phase II TACTI-002 trial was one of only nine abstracts selected by SITC to be showcased at the SITC 2022 Press Conference out of over 1,500 abstracts submitted for SITC 2022.



Data from first line non-small cell lung cancer patients in Immutep Limited's Phase II TACTI-002 trial was selected for a prestigious Oral Presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting.

## Keynote address at first ever LAG-3 focused conference

2022 LAG-3 Targeted Drug Development Summit, CEO Marc Voigt delivered opening remarks and Frederic Triebel gave the keynote address.





## Benchmarking against Pembrolizumab Monotherapy: Strong ORR/PFS Across Entire PD-L1 Spectrum vs Pembrolizumab

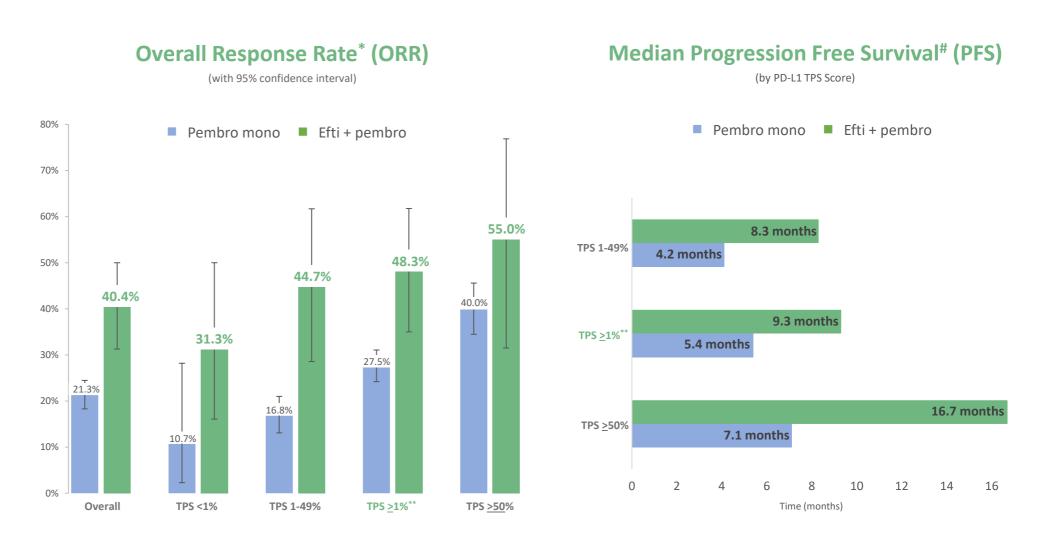




TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

#### **Key Takeaways**

- Superior ORR/PFS across all PD-L1 levels vs pembrolizumab monotherapy
- Promising interim mPFS: 6.6 months overall and 9.3 months PFS in TPS >1%
- Efti has potential to substantially increase # of patients responding to anti-PD-1 therapy



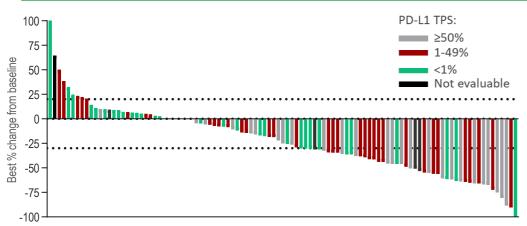
<sup>\*\*</sup> Efti + Pembro Fast Track Designation in PD-L1 >1%

## Deep and Durable Responses

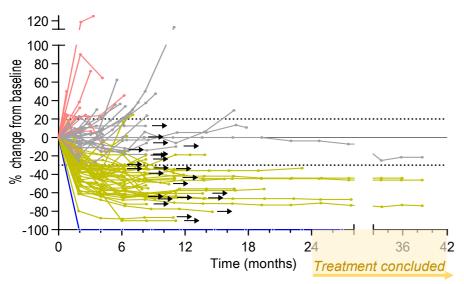


TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

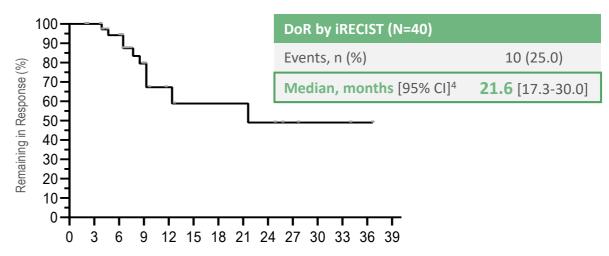
#### **Tumor Burden Reduced in Majority of Patients**



#### Change in Tumor Size Over Time<sup>1</sup>



#### Interim Median Duration of Response (DoR)



- Responses are deep and across all PD-L1 subgroups
- Response onset is early & responses are long-lasting: strong interim mDoR 21.6 months
- ~70 % of patients have a decrease of target lesions
- Less than 10% of responding patients progress within 6 months

## IO + IO + Chemo Combination Trial (INSIGHT-003)





INSIGHT-003: Phase I in Solid Tumors Focusing on NSCLC Adenocarcinomas

#### INSIGHT-003 - Third arm (Stratum C) of ongoing investigatorinitiated study focusing on NSCLC adenocarcinomas





- Evaluating triple combination therapy consisting of efti in conjunction with carboplatin/pemetrexed & anti-PD-1 therapy
- Trial assessing safety, tolerability and initial efficacy
- 14 of 20 metastatic NSCLC patients have been enrolled<sup>1</sup>
- Majority of patients have PD-L1 TPS <50%
- Triple combination well tolerated & appears to be safe
- Promising early results with 72.7% response rate and 90.9% disease control rate in evaluable (N=11) 1st line NSCLC patients

#### **Initial Efficacy**

| Tumour Response according to RECIST 1.1 (N=11) | N, (%)     |
|--|------------|
| Complete Response (CR)                         | 0 (0)      |
| Partial Response (PR)                          | 8 (72.7%)  |
| Stable Disease (SD)                            | 2 (18.2%)  |
| Progressive Disease (PD)                       | 1 (9.1%)   |
| Objective Response Rate (ORR)                  | 8 (72.7%)  |
| Disease Control Rate (DCR)                     | 10 (90.9%) |

81.8 % patients had PD-L1 TPS < 50% with ORR of 66.7 %

#### **Interim Safety**

| Safety Parameter (N=14)                                   | N, (%)    |  |
|---|-----------|--|
| Most Frequent AEs   | 1 (9.1)   |  |
| Neutrophil count decreased (grade 1-4)                    | 11 (78.6) |  |
| White blood cell decreased (grade 1-4)                    | 9 (64.3)  |  |
| Platelet count decreased (grade 1-3)                      | 8 (57.1)  |  |
| Anemia (grade 1-3)  | 8 (57.1)  |  |
| Patients with at least one SAE                            | 4 (28.6)  |  |
| Patients with at least one SAE related to study treatment | 1 (7.1)   |  |
| No now cafety signals detected thus for                   |           |  |

"Efti has accumulated an excellent safety profile to date, driving its high suitability for combination with standard of care therapies to address areas of unmet need for cancer patients. INSIGHT-003 represents the first triple combination therapy consisting of efti plus anti-PD-1 and chemo, and we are pleased with these promising, early results." - Prof. Dr. Salah-Eddin Al-Batran, Lead Investigator

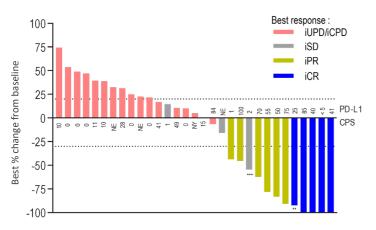
## 2L HNSCC: Robust ORR/CR with Long-Lasting Efficacy



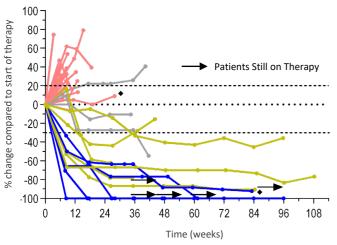


TACTI-002/KEYNOTE-798: 2<sup>nd</sup> Line Head & Neck Squamous Cell Carcinoma (Part C)

#### Responses at all PD-L1 levels including 5 iCRs



#### **Deep and durable responses**



|                               | Efti + Keytruda<br>Combination* | Keytruda<br>Monotherapy# |
|-------------------------------|---------------------------------|--------------------------|
| Clinical Trial & Phase        | P2 (TACTI-002/KN-798)           | P3 (KN-040)              |
| Patient Number / tumor type   | 39 / 2L HNSCC                   | 247 vs. 248 / 2L HNSCC   |
| PD-L1 Status                  | PD-L1 All comer                 | PD-L1 All comer          |
| Complete Response (CR) %      | 13.5%                           | 1.6%                     |
| Partial Response (PR) %       | 16.2%                           | 13%                      |
| Stable Disease (SD) %         | 8.1%                            | 22.7%                    |
| ORR in evaluable patients %   | 35.5%                           | n/a                      |
| Overall Response Rate (ORR) % | 29.7%                           | 14.6%                    |
| PD-L1 CPS ≥1% group           | 40.7%                           | 17.3%                    |
| PD-L1 CPS ≥20% group          | 64.3%                           | 21.9%                    |
| Median PFS (months)           | 2.1                             | 2.1                      |
| PD-L1 CPS ≥1% group           | 4.1                             | 2.2                      |
| Median OS (months)            | 12.6                            | 8.4                      |
| PD-L1 CPS ≥1% group           | 12.6                            | 8.7                      |

Eight-fold increase in CR with efti + pembro

More than double ORR across all PD-L1 levels with efti + pembro

50% increase in mOS

## Targeting 1L HNSCC with Fast Track Designation (TACTI-003)





TACTI-003: Phase IIb in 1st Line Head and Neck Squamous Cell Carcinoma (HNSCC)



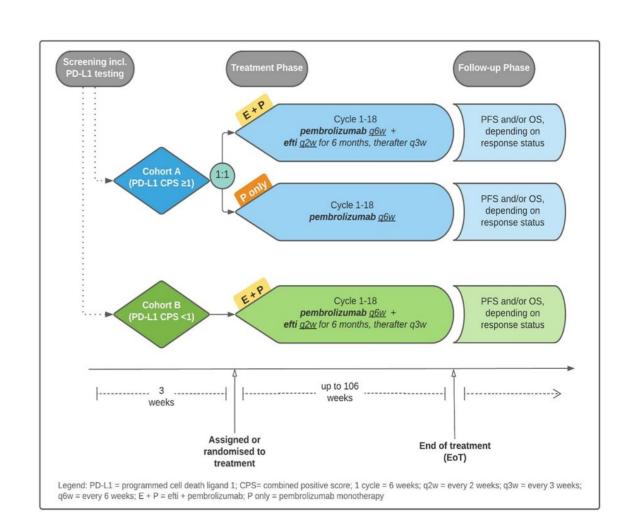


#### Design:

- Randomised trial with ORR as primary endpoint
- Sites worldwide (AU, US, Europe)
- Approximately 154 patients: either to be randomized to have sufficient patients in each group or in an experimental arm

#### **Status:**

- Received FDA Fast Track on strength of TACTI-002 data in 2L HNSCC
- ✓ Recruiting: ~38% enrolled; new sites activated & enrollment increasing\*
- ✓ Independent Data Monitoring Committee (IDMC) recommended continuing trial with no modifications after review of initial safety data; also reviewed initial efficacy data yet was not primary focus of analysis
- ✓ Trial in Progress abstract presented at SITC 2022



## AIPAC Phase IIb: Driving OS Improvement with Superior QoL





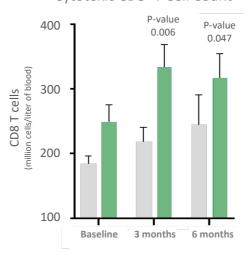
AIPAC: Active Immunotherapy PAClitaxel in HER2-/ HR+ metastatic breast cancer Phase IIb Trial

AIPAC: Multicenter, placebo-controlled, double-blind, 1:1 randomized Phase IIb study; 226 patients randomized to efti (N=114) or placebo (N=112)

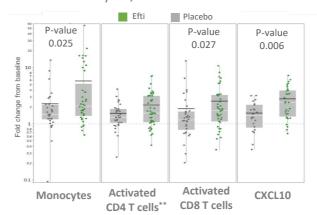
| Pre-specified Subgroups | Median Overall Survival | Hazard Ratio | P-value |
|-------------------------|-------------------------|--------------|---------|
| Low Monocytes           | +19.6 months mOS        | HR 0.44      | p=0.008 |
| Under 65 Years          | +7.5 months mOS         | HR 0.66      | p=0.017 |
| Luminal B               | +4.2 months mOS         | HR 0.67      | p=0.049 |

- ✓ Efti + paclitaxel combination:
  - Led to significant OS improvement in three pre-specified subgroups: low monocytes, under 65 years, & luminal B
  - ORR & DCR of 48.3%/85.1% vs placebo 38.4%/75.9%
- ✓ Based on encouraging clinical data and high unmet need to improve OS while maintaining QoL, metastatic breast cancer (MBC) remains an attractive opportunity
- ✓ Immutep's preparations for future clinical development in MBC, including engagement with regulators, CROs & other stakeholders, are progressing

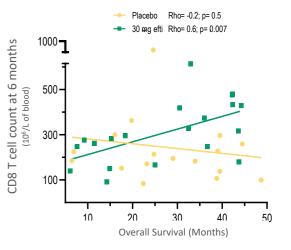
## Statistically-Significant Increase of Cytotoxic CD8<sup>+</sup> T Cell Count



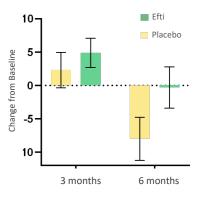
#### Statistically-Significant Increase in Monocytes, CD8+ T Cells & CXCL10



#### Statistically-Significant Correlation: OS & Cytotoxic CD8<sup>+</sup> T cell count



Sustained Quality of Life\*



## Clinical Development Strategy for Efti



Encouraging clinical data supports broad therapeutic potential of efti - optionality to progress development in multiple indications.

## Prioritising 1st line NSCLC

- Planning and regulatory interactions ongoing
- Late-stage trial design informed by ongoing INSIGHT-003 trial and maturing TACTI-002 data
- Fast track designation

## Ongoing development in 1st line HNSCC

- Ongoing Phase IIb TACTI-003 trial
- FDA Fast Track designation

## Future development in metastatic breast cancer

 Continuing preparations for late stage development: engagement with regulators, CROs and other stakeholders

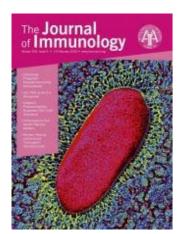
## Continued expansion of efti in additional indications and combinations

 Last example: soft tissue sarcoma trial

Immutep, or its partners, aim to obtain marketing authorisation in multiple indications to fully exploit the potential of efti with its unique mechanism of action

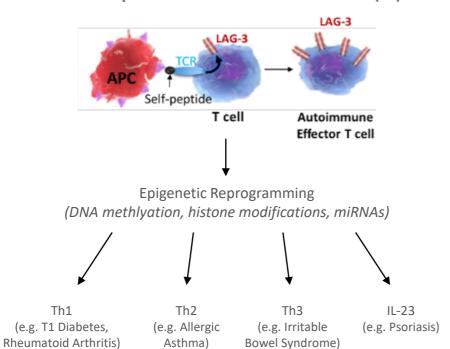
## IMP761: Broad Potential Targeting Auto-Reactive Memory T Cells immuter





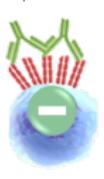
A LAG-3-Specific Agonist Antibody for the Treatment of T Cell -Induced **Autoimmune Diseases** Mathieu Angin, Chrystelle Brignone and Frédéric Triebel J Immunol January 6, 2020, ji1900823

#### Deficiency in LAG3 Pathways Linked to **Development of Autoimmune Diseases (AI)**



#### **IMP761**

Immutep's proprietary humanized IgG4 LAG-3—specific antibody



As the **first LAG-3**—**specific agonist** acting upstream on activated T cells, the root cause of self-Ag-specific T cell-induced disease, IMP761 is a **potential game-changer** in autoimmune diseases.

#### Novel Small Molecule Anti-LAG-3 Collaboration







Collaboration established in 2019 combining Immutep's deep LAG-3 biology experience and expertise of world leading scientists at Cardiff University

"We are delighted to collaborate with Immutep on this important project to develop a **small molecule anti-LAG-3** treatment for cancer patients that could offer the **convenience** of a tablet or capsule at a fraction of the cost of existing anti-LAG-3 candidates."

Professor Andrew Godkin, Theme Lead in Immunology in the College of Biomedical Life Sciences, Cardiff University

#### **Key Financials**





Revenue and other income increased mainly due the recognition of a net gain in FX of A\$1.2M and an increase in R&D tax rebates. A\$4.5M from the Australian and French governments was recognised in FY22 compared to A\$3.4M in FY21.



R&D and IP expenses significantly increased as expected due to the increased clinical trial activity for TACTI-003 and increased manufacturing activities



Strengthened cash balance with A\$67.2 million two-tranche placement and share purchase plan (Share purchase plan and tranche two placement completed in July 2021)



Loss after tax for FY22 was higher compared to FY21 mainly due to the increase in R&D expenses

|  | FY22     | FY21     |
|--|----------|----------|
| Revenue and other income                                   | A\$6.8M  | A\$4.0M  |
| G&A Expenses   | A\$7.2M  | A\$6.3M  |
| R&D and IP expenses  | A\$31.3M | A\$17.2M |
| Net loss   | A\$32.2M | A\$29.9M |
| Net operating cash outflow                                 | A\$30.2M | A\$17.6M |
| Cash and cash equivalents at the end of the financial year | A\$80.0M | A\$60.6M |
| Cash and cash equivalents at 30<br>September 2022          | A\$73.9M |          |

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#### Milestones ahead



#### 2022

- Year to date:
  - ✓ 1L NSCLC Oral Presentation at ASCO (TACTI-002; Part A)
  - ✓ 2L NSCLC PD-X refractory data at ELCC & WCLC 2022 (TACTI-002; Part B)
  - Fast Track Designation granted in 1L NSCLC
  - New, significant data from AIPAC study
  - IP expansion for eftilagimod alpha
  - New data from Phase II TACTI-002 in 1L NSCLC at SITC 2022
  - Initial results from INSIGHT-003 (triple-combo) at SITC 2022
  - ✓ Trial in progress poster on randomized trial in 1L HNSCC at SITC 2022
- Expansion of existing programs (i.e., new sarcoma trial)
- Regulatory updates
- Manufacturing scale up to 2,000L
- Updates on IMP761 & partnered programs

#### 2023

- TACTI-003 updates and top line readout
- TACTI-002 data updates
- INSIGHT-003 updates and readout
- Start soft tissue sarcoma study
- Preparations for late-stage development in NSCLC
- Preparations for late-stage development in MBC
- Manufacturing updates (e.g. comparability)
- Regulatory updates (e.g. FDA, EMA)
- Expansion of the clinical trial pipeline
- Preclinical development of IMP761
- Update from partnered programs
- Partnering updates

## **Corporate Snapshot**



Pioneering LAG-3 portfolio in oncology and autoimmune diseases with four product candidates in multiple clinical trials

- First-in-class positioning with eftilagimod alpha (efti)
- Multiple big pharma partnerships & collaborations,
   while retaining full control of efti (ex-China) & IMP761
- Well funded with ~A\$73.9 million\* in cash
- Cash runway to H1 CY2024\*
- Market cap ~A\$264M / ~\$175M US\*\*
- Ticker symbols: IMM (ASX) & IMMP (NASDAQ)
- Total institutional ownership of ~57% includes:
  - Fidelity (FIL Ltd.) ~7.41%
  - Australian Ethical ~4.98%\*\*\*

Analyst research coverage





















Thank You