

## Immutep Ltd.

### New Age Immune Regulator; Initiate with a Buy Rating and \$8.30 Price Target

IMMP (NASDAQ)

#### Company & Market Data

Closing Price (as of 08/02/2021):	\$3.46
Rating:	BUY
Price Target:	\$8.30
52 Week Range:	\$1.22 - \$7.95
Shares Outstanding (MM):	85.1
Market Capitalization (MM):	\$294
Fiscal Year End:	Dec

#### Estimates

EPS	2020A	2021E	2022E
1Q	—	—	—
2Q	—	—	—
3Q	—	—	—
4Q	—	—	—
Full Year	\$(0.33)	\$(0.59)	\$(0.56)
Revenue (MM)	2020A	2021E	2022E
1Q	—	—	—
2Q	—	—	—
3Q	—	—	—
4Q	—	—	—
Full Year	\$13.7	\$4.3	\$5.0

#### Ratios

P/E	NA	NA	NA
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\*Revenue (MM): In \$AUD

\*EPS: In \$AUD



Chart data: Bloomberg

**We are initiating coverage on Immutep (NASDAQGM: IMMP) with a Buy rating and \$8.30 price target.** Immutep is a clinical-stage immuno-oncology company focused on developing LAG-3 therapeutics for oncology and autoimmune diseases. The lead asset eftilagimod alpha (efti) paired with PD-1/PD-L1 agents is currently evaluated in metastatic breast cancer (mBC), non-small-cell lung carcinoma (NSCLC), head and neck squamous cell carcinoma (HNSCC), and other solid tumors. The second asset IMP761 is at the preclinical stage for autoimmune disease. As the LAG-3 is drawing much attention as a target following Bristol Myers Squibb's (BMY, \$68, Not Rated) positive pivotal data readout, Immutep's efti also made its place in the LAG-3 arena. We would like to emphasize the distinct mode of action of efti, a soluble LAG-3 agonist and an MHC II activator. We like Immutep's diversified portfolio in multiple indications and disease areas (NSCLC, HNSCC, BC, and inflammatory diseases), partnership portfolio (GSK, Novartis, IKF, and others), and the data obtained from the Phase 2 TACTI-002 study in 2nd line HNSCC and 1st line NSCLC (ORR 30% and 42%, respectively) and from Phase 2b AIPAC study in mBC (2.7 mos of OS benefit). In our view, the Australian biotech Immutep is one of the most diversified LAG-3 therapeutics/APC activators play in the public market.

**Value-driving events on the calendar.** (a) We expect to have a thorough look at the final data from the AIPAC study (2nd OS follow-up in mBC) in 2H21. (b) We expect clarity on the next steps for NSCLC in 2022. We believe that would potentially generate additional value for the company. (c) We will be on the watch for the interim data analysis of TACTI-003 in 1st line HNSCC in 2022 after commencement of trial in YE 2021. (d) We also look for regulatory engagement, further information on partnerships, and updates on the IMP761 program. We will pay special attention to data on differentiation from competitor agents and activity across various targets and combinations in the evaluated disease landscapes.

**Our valuation.** We value Immutep using a risk-adjusted discounted cash flow model. We base our valuation on HNSCC and mBC markets as the company intends to advance these two indications in the clinic and view other clinical programs (NSCLC) and the preclinical pipeline as potential upside. We took a top to bottom approach and used PD-1/PD-L1 agents WW sales in these two indications and applied a propitiate market penetration for the efti/PD-1 combination. And, we assign a 50% probability of success in these indications. Using the Gordon Growth Method, we calculate a terminal value of \$2.01 billion and arrive at our \$8.30 price target.

**Risks.** Risks include: 1) currently the company is solely depending on efti's success in multiple indications, 2) clinical data is compelling; however, the indications that are assessed by IMMP are highly competitive/crowded landscapes, 3) emerging new treatment regimens can change the treatment paradigm and impact the stock valuation.

Disclosures and Analyst Certifications can be found in Appendix A.

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Member: NYSE, NYSE American, NYSE Arca, FINRA, all other principal exchanges and SIPC

## Investment Thesis

We recommend shares of IMMP based on our current key investment thesis listed below:

- In our view, the LAG-3 MHC II activator mechanism presents a frontier therapeutic approach with compelling underlying biology, validated safety and efficacy, and opportunities to bridge current gaps for clinical success.
- We see Immutep has demonstrated a compelling efficacy/safety profile and pipeline that may potentially help address some of the current gaps for PD-1/PD-L1 treatment. The company showed highly competitive clinical results in multiple indications including HNSCC, NSCLC, and mBC.
- We believe i) upcoming AIPAC study (2nd OS follow-up in mBC) readout in 2H21, then, advancement of this program in the clinic in 2022, ii) commencement of TACTI-003 trial in 1<sup>st</sup> line HNSCC, followed by interim data readout in 2022 will be potential significant near- and medium-term potential catalysts.
- In our view, Immutep's pipeline presents potential large upside with HNSCC, mBC, and NSCLC programs targeting unmet medical needs with larger market potential in these indications.
- Given the current market cap of \$362 mm, we see attractive value creation and upside potential for IMMP stock, with also upcoming key potential catalysts in 2H21/1H22.

### What do we like?

**Clinical data showed a compelling synergistic effect of efti coupled with PD-1/PD-L1 agents.** We guide investors to pay attention to the distinct mode of action of efti versus other LAG-3 antagonist agents. As we like the recent developments in the LAG-3 arena, where it became the 3<sup>rd</sup> validated target after PD-1 and CTLA-4 with the ASCO readout from Bristol Myers Squibb's pivotal study (RELATIVITY-047), we do not think Immutep's efti should be classified as a LAG-3 antagonist agent. Efti is derived from the soluble form of the lymphocyte-activation gene 3 (LAG-3) fused to the four extracellular Ig domains of LAG-3 to the Fc portion of human IgG1. It is a recombinant soluble LAG-3Ig fusion protein that binds to MHC class II with high avidity. Efti acts as an MHC II agonist and mediates antigen-presenting cell (APC) and then antigen-experienced memory CD8+ T cell activation, unlike the other LAG-3 targeting agents (LAG-3 antagonist) that bind to and inhibits LAG-3, hence LAG-3 inhibitory signaling pathway. While it could potentially act like an antagonist and compete with the LAG-3 binding to MHC II at high concentrations, at the selected clinical concentrations, efti works as an MHC II activator. As we get into details on the mechanism of action of efti in this report, noting that efti is not a LAG-3 antagonist agent, the most compelling key factor why we like efti is the clinical benefit observed with the efti/pembrolizumab (pembro) combination. Efti coupled with pembro demonstrated 29.7% of overall response rate (ORR) including 5 complete responses (CR) and 37.8% diseases control rate (DCR) in 37 HNSCC patients. Among selected PD-L1 expression (CPS $\geq$ 1), median OS (58% events) was 12.6 months, median PFS (71% events) was 4.1 months and ORR was 45.8% (95% CI) in HNSCC. The results were favorable and exceeded Keytruda monotherapy data (2<sup>nd</sup> line HNSCC: 16% of ORR rate in 2016 and 1<sup>st</sup> line HNSCC: the median OS was 13.0 months for the pembrolizumab plus chemotherapy arm and 10.7 months for the cetuximab plus chemotherapy arm (HR 0.77; 95% CI: 0.63, 0.93; p=0.0067). While we only highlight HNSCC data in this section, we think the results in NSCLC and mBC patients were also remarkable. In our view, the clinical benefit generated by the efti/pembro combination is solid and compelling.

**Billion-dollar market opportunity.** PD-1/PD-L1 agents are posed as a backbone therapy in the approved indications. Anti-LAG-3 will be positioned as an additive to these agents, paired with anti-PD-1/PD-L1 agents. PD-1/PD-L1 agents reached \$14.4 billion in 2020 and are estimated to grow to \$64.3 billion in 2026 (based on Evaluate Pharma). Immutep focuses on two indications i) HNSCC a relatively smaller market (predicted to reach ~\$2.6

billion in 2026) with a potentially accelerated path to approval, ii) breast cancer with larger market potential, estimated to reach \$4.4 billion in WW sales in 2026 (based on Evaluate Pharma). On the commercial prospects of anti-LAG-3, we believe the opportunity is immense.

**Eclectic pipeline.** In our view, Immutep is one of the most diverse players in the LAG-3 arena. The company has shown compelling data in multiple indications. Immutep is not only pursuing multiple opportunities in cancer including head and neck squamous cell carcinoma (HNSCC), metastatic breast cancer, and non-small cell lung cancer (NSCLC) but also in advanced stages of development versus competitors and also tapping into autoimmune disease. Established collaborations and partnerships are also noteworthy including Merck KGaA (MKGAF, \$208.3, Not Rated), Novartis (NVS, \$92.3, Not Rated), GSK (GSK, \$40.2, Not Rated), and others.

#### **Where do we see vulnerabilities?**

**APC activators have shown mixed clinical efficacy.** Although efiti is unique as it is the only soluble LAG-3 (LAG-3 agonist)/APC activator, i) it is not a validated target or mechanism like the LAG-3 antagonist mechanism, and ii) multiple other immune stimulator agents recently showed lackluster clinical benefit in patients. Toll-like receptors (TLRs, e.g., tilosotolimod) and STING agonists (e.g., MK-1454 and ADU-S100) are APC activators, and both classes of drug candidates demonstrated underwhelming efficacy in the clinic. We think there is skepticism in the APC activator field. While the efforts continue, we also recognize that it became somewhat common to learn from the failures of the 1<sup>st</sup> generation drug candidates and i) improve and obtain more potent 2<sup>nd</sup> generation versions, ii) find the right market or indications with iii) the right combination strategy in the I/O space.

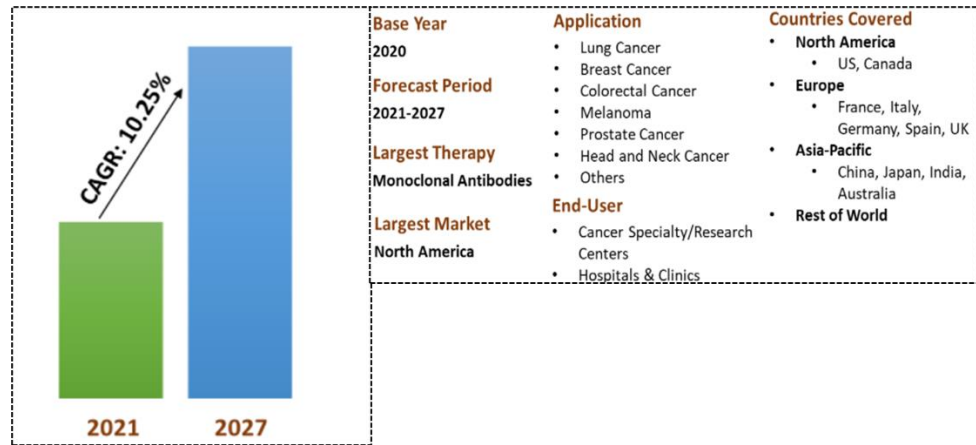
**Highly crowded field.** The company is assessing efiti in large, hence highly compelling, and crowded diseases landscapes such as non-small cell lung cancer (NSCLC), metastatic breast cancer, head, and neck cancer (HNSCC). The developmental pipeline is very crowded with many variations of combinations and targets: I/O-I/O, I/O-targeted therapy, I/O-chemotherapy, and others. We see multiple layers to the competition with many attributes including i) the approval timeline (first to market), ii) market positioning (which combination(s) and what line of treatment), and iii) market penetration (approval timing, distinct efficacy, or safety profile, favorable dosing schedule or others). Therefore, Immutep's data and strategy on how to position efiti in these dynamic disease landscapes will play a key role in a successful approval strategy and commercialization.

**One lead asset, the rest is overdue.** While we like the diversity of the pipeline and the partnership portfolio, we are on watch to see data from the partner Novartis on the LAG525 (IMP702, a LAG-3 antagonist) program. The other partner GSK halted a clinical trial in ulcerative colitis. We are waiting to see advancement and data from autoimmune disease programs and other assets beyond efiti.

### Industry Overview

Immutep is a clinical-stage biotechnology company focused on developing cancer immunotherapies and immunosuppressants. The company has a diverse portfolio that is currently being explored in a variety of solid tumors and autoimmune diseases. Spending on cancer treatment is expected to reach \$187 billion worldwide and to increase to approximately \$273 billion by 2025, 12% CAGR, based on Evaluate Pharma. Based on Evaluate Pharma’s estimates, oncology is expected to contribute 21.7% of total pharmaceutical sales in 2026, 66% of sales are anticipated to derive from immuno-oncology agents and protein kinase inhibitors. The global cancer immunotherapy market is set to grow at a CAGR of 10.25% between 2021 and 2027.

**Exhibit 1. The global cancer immunotherapy market is expected to grow at a CAGR of 10.25% from 2021-2027 to reach USD 174.33 billion by 2027**



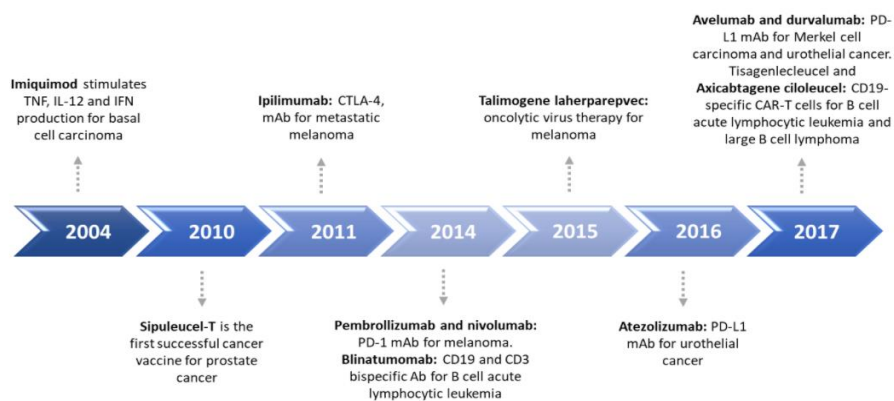
Source: UnivDatos Market Insights and Ladenburg Thalmann Research

The last decade has been revolutionary for cancer treatment through advancements in targeted therapy, immunotherapy, and combinational regimens. Extensive sample pools and clinical data in combination with advanced sequencing tools have provided a broad understanding of tumor genetic background and evolution. Although tailoring drugs to target the driving oncogenic mutations was a promising strategy, researchers came to an understanding that cancer is constantly evolving and adapting. Therefore, in recent years cancer research has been focused on the universal system -- immune cells for anti-cancer activity. An immune response is a multiple-step process and involves coordination across various cell types and tissues including tumor cells, antigen-presenting cells, and T-cells. The majority of the recent research focuses on activating, priming, and regulating T-cells, because of their ability for selective recognition of peptides/antigens and killing of antigen-presenting cells. The discovery and approval of checkpoint inhibitors have been significant for the evolving oncology landscape shifting toward immuno-oncology development. immuno-oncology agents have shown favorable results of increased survival and decreased toxicity.

Naïve T-cells are differentiated and activated into effector T-cells. Under constant antigen exposure such as in cancer, T-cell differentiation is in an altered state (so-called T-cell exhaustion) causing T-cells to function poorly. Immune checkpoints are negative regulators (inhibitory receptors) of the effector T-cells and conserve expression of these receptors, a hallmark of T-cell exhaustion. Cancer cells utilizing checkpoint molecules causing T-cell exhaustion and deceived as normal cells result in suppression of immune attack. Immune checkpoint inhibitors targeting checkpoint molecules, such as cytotoxic T-

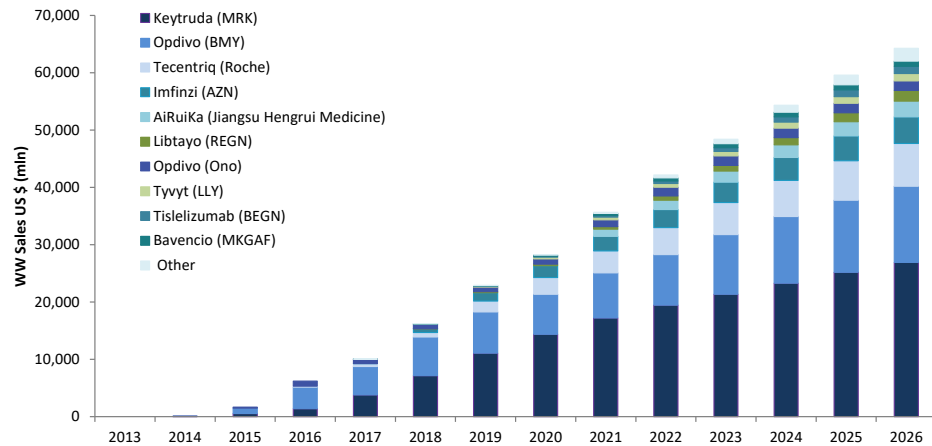
lymphocyte associated protein 4 (CTLA4) and T-cell programmed cell death protein 1 (PD-1) and its ligand PD-L1, block this inhibitory signal resulting in activation of T-cells and anti-tumor activity. Yervoy (anti-CTLA4) was the first major blockbuster drug in the field of immunotherapy as a treatment for unresectable or metastatic melanoma in 2011. Following Yervoy, checkpoint inhibitors that either bind to the programmed death 1 receptor (PD-1) or one of its ligands (PD-L1) were approved in 2014, the most widely indicated and prescribed of which are Bristol-Myers Squibb's Opdivo (nivolumab) and Merck's Keytruda (pembrolizumab).

## Exhibit 2. Timeline of FDA-approved cancer Immunotherapies



Source: UnivDatos Market Insights

The first two PD1/PD-L1 inhibitors were approved in 2014 (Keytruda's approval in September was followed by Opdivo's approval in December). There are currently over ten PD1/PD-L1 inhibitors approved in numerous indications including melanoma, non-small cell lung cancer and (NSCLC), renal cell carcinoma (RCC), head and neck cancer, Hodgkin's lymphoma, bladder cancer, Merkel cell carcinoma, colorectal cancer, gastric cancer, hepatocellular (liver) cancer (HCC), cervical cancer, diffuse large B-cell lymphoma (DLBCL), small cell lung cancer (SCLC), squamous cell carcinoma (SCC), breast cancer, esophageal cancer, and others. Keytruda has become a blockbuster drug, dominating the cancer market as the top-selling medicine in the space. Keytruda's worldwide (WW) sales in 2020 reached \$14.4 billion. By 2026, Evaluate Pharma projects \$64.3 billion of total sales of PD1/PD-L1 inhibitors, \$26.9 billion (42% of total PD1/PD-L1 WW sales) sales from Keytruda alone (Exhibit 3).

**Exhibit 3. Worldwide (WW) sales of anti-PD-1/PD-L1 agents (in \$ US)**

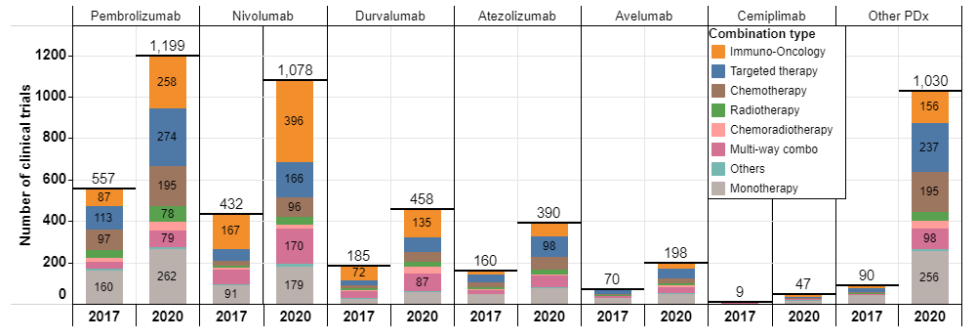
Source: Evaluate Pharma and Ladenburg Thalmann Research

The overall demand is being propelled by a paradigm shift from conventional chemotherapies and toward immunotherapies. Among application types, lung cancer accounted for the largest share in 2020 and is expected to grow at a 9.92% CAGR during the forecast period 2021-2027. The breast cancer segment is anticipated to grow at the highest CAGR during the analyzed period and is expected to account for a revenue share of almost 20.71% by 2027.

Despite checkpoint inhibitors have demonstrated unprecedented clinical activity across a range of cancers, the clinical benefit is only observed in some patients. Based on a study [published](#) in JAMA Network Open suggests that although approximately 44% of cancer patients may be eligible to be treated with one of the checkpoint inhibitors currently on the market, only about 13% will respond to treatment. Biomarker identification to predict responders or select patients has been challenging. Furthermore, 50% of patients who respond to therapy develop resistance to treatment with PD1/PD-L1 agents.

Therefore, the scientific community continues its efforts to develop more effective treatment methodologies using combinational regimens. Experts agree on PD1/PD-L1 agents remain as the backbone of treatment. There are multiple combination approaches underway, including combination with chemotherapy, targeted therapy, secondary checkpoint inhibitors, oncolytic viruses, and vaccines. The efforts have been focused on finding the right combination partner with significant synergy and a favorable safety profile to provide greater clinical benefit for the patients.

**Exhibit 4. PD-1/PD-L1 clinical trial landscape**



Source: cancerresearch.org

### Company Overview

Immutep is a clinical-stage biotechnology company focused on the development of immune checkpoint LAG-3 (Lymphocyte Activating 3) therapeutics for oncology and autoimmune diseases. The lead asset Eftilagimod Alpha (efti or IMP321) is being assessed in combination with PD-1/PD-L1 agents or chemotherapy in numerous clinical trials in metastatic breast cancer, non-small-cell lung carcinoma (NSCLC), head and neck squamous cell carcinoma, solid tumors, melanoma, and Covid-19 diseases. The second asset IMP761 is at the preclinical stage for autoimmune disease.

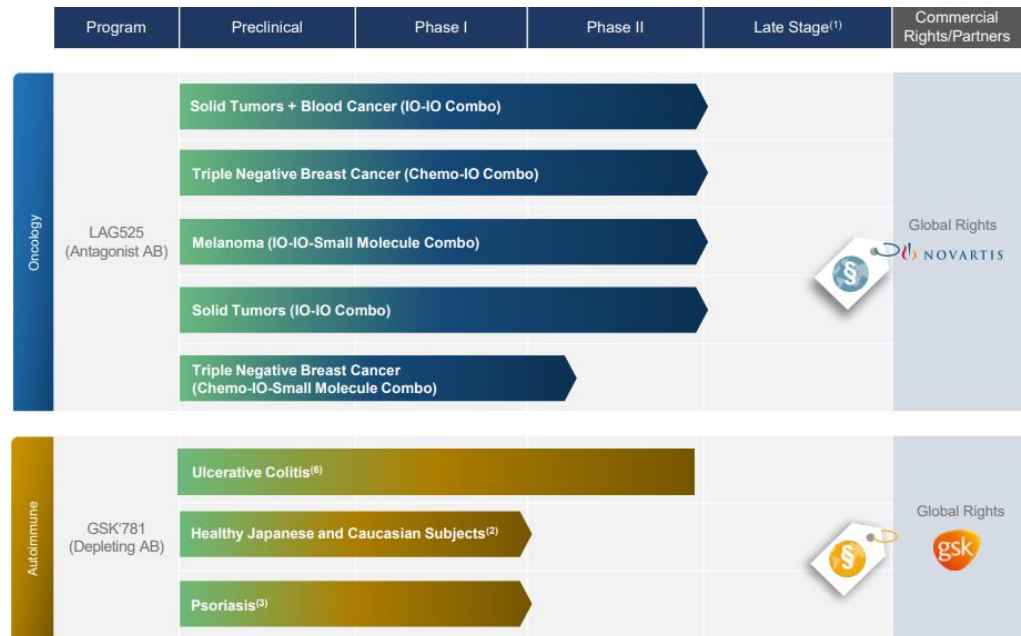
### Exhibit 5. Company's pipeline



Source: Company SEC filings



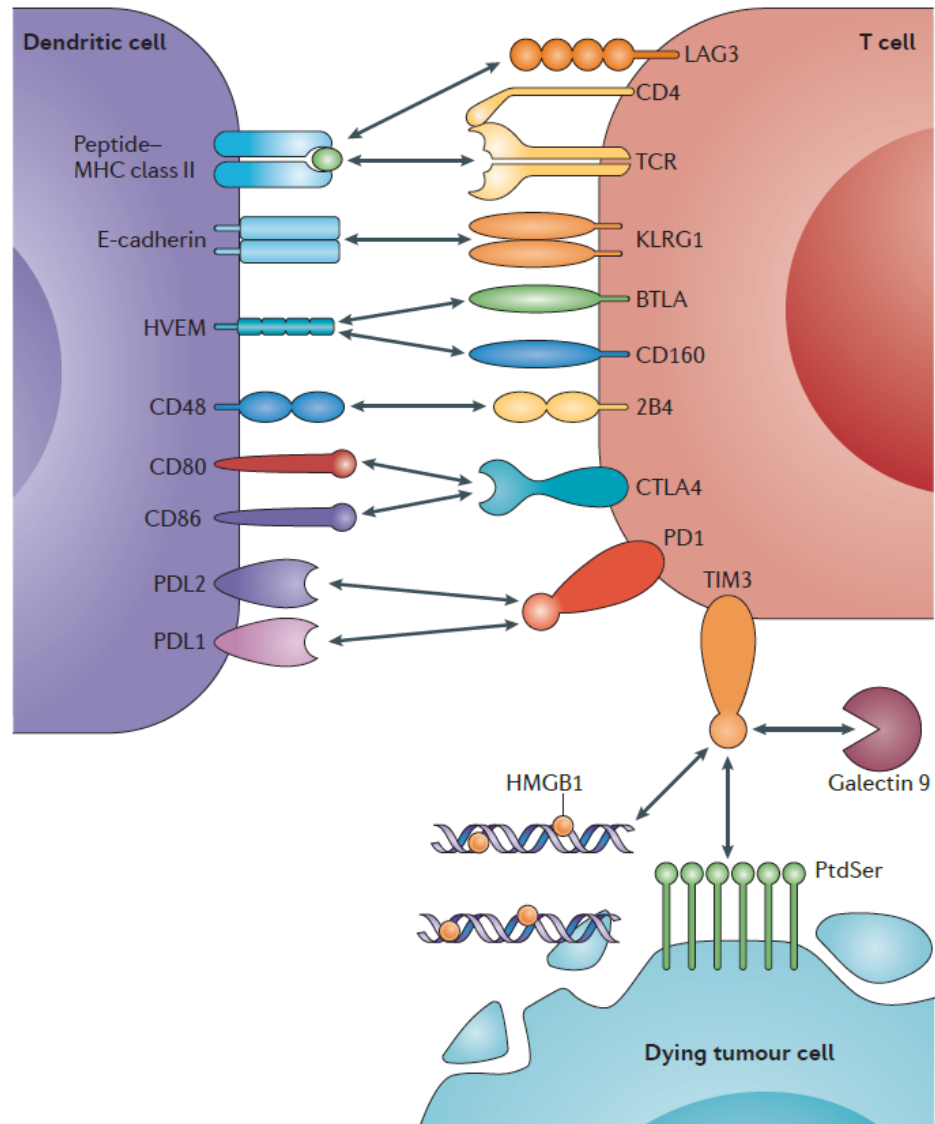
**Exhibit 6. Out-licensed immunotherapy pipeline**



Source: Company SEC filings and Ladenburg Thalmann research

**Immune checkpoint LAG-3 targeting in oncology – LAG-3 antagonist**

LAG-3 is among the negative regulator of T-cell receptors including PD-1, T cell immunoglobulin domain, and mucin domain 3 (TIM3), B and T lymphocyte attenuator (BTLA), and others. Expression of these inhibitory receptors was shown to be associated with compromised function of antigen-specific T cells in patients with chronic infection or cancer. Blocking LAG-3 and other inhibitory receptors can restore human T cell function.

**Exhibit 7. Key Immune checkpoints**

Source: *Nature Reviews, immunology, Volume 15, January 2015*

**LAG-3**

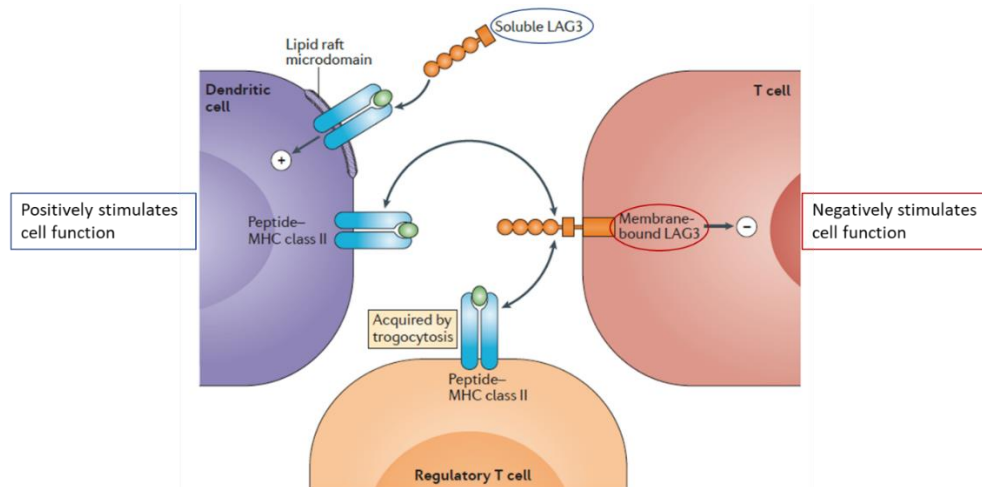
- is a novel transmembrane protein,
- binds to major histocompatibility complex (MHC) class II as a ligand,
- is mainly expressed in activated T and natural killer (NK) cells and was identified as a marker for the activation of CD4+ and CD8+ T cells,
- found on tumor-infiltrating regulatory T cells (Tregs) in many types of cancer when compared with non-malignant peripheral cells,
- plays pivotal roles in autoimmunity, tumor immunity, and anti-infection immunity.

LAG-3 binds MHC class II molecules with high affinity and the human *LAG-3* gene has 20% identity with the *CD4* gene. While LAG-3 is not expressed by resting T cells, it is upregulated several days after T cell activation. It is also upregulated on exhausted T cells compared with effector or memory T cells and is expressed on activated Treg cells at higher levels than on effector T cells.

It comes as no surprise LAG-3 function and mechanism of action are complex and can stimulate positively or negatively cell function. A spliced variant of the LAG-3 gene is translated to a soluble form of LAG-3, which promotes Immune activity. LAG-3 interaction with the MHC class II ligands can be insoluble or membrane-bound form depending on the alternative splice variants.

- i) Signaling through membrane-bound LAG-3 on T cells after it binds to MHC class II molecules negatively regulates T cell function.
- ii) Conversely, signaling through MHC class II in lipid raft microdomains on a subset of dendritic cells after it is bound by soluble LAG-3 (sLAG-3) results in dendritic cell activation.
- iii) LAG-3 is also reported to bind to MHC class II molecules that have been acquired by regulatory T cells in the process of trogocytosis.

#### Exhibit 8. Membrane-bound versus soluble LAG-3

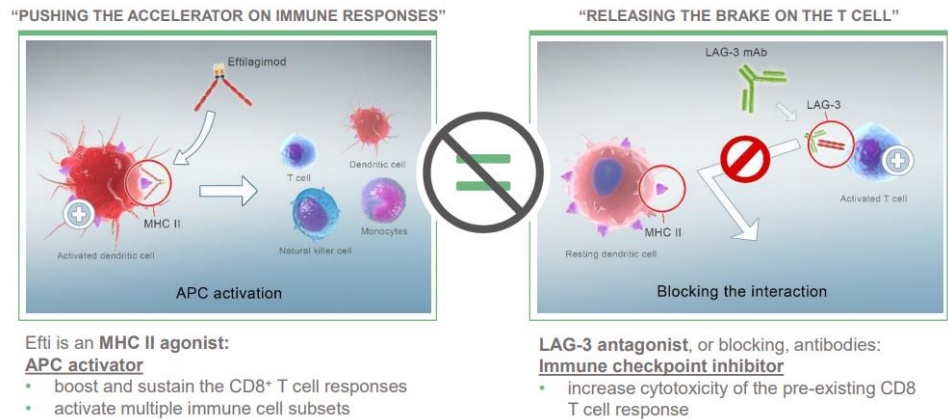


Source: *Nature Reviews, immunology, Volume 15, January 2015*

LAG-3 is the third validated target in the clinic following PD-1 and CTLA-4. Preliminary results of LAG-3 blockade in melanoma and other cancers are compelling, particularly in combination with Immune checkpoint inhibitors (PD-1) blockade for refractory patients.

#### Mechanism of action of efti is distinct from other LAG-3 antagonists

Immutep's efti derived from the soluble form of the lymphocyte-activation gene 3 (LAG-3) fused the four extracellular Ig domains of LAG-3 to the Fc portion of human IgG1. It is a recombinant soluble LAG-3Ig fusion protein that binds to MHC class II with high avidity. Efti acts as an MHC II agonist and mediates antigen-presenting cell (APC) and then antigen-experienced memory CD8+ T cell activation, unlike the other LAG-3 targeting agents (LAG-3 antagonist) that bind to and inhibits LAG-3, which is an Immune checkpoint.

**Exhibit 9. Efti has a distinct mechanism of action compared to LAG-3 antagonists**

Source: Company SEC filing

The most important phenomenon to recognize is the difference between Immutep's efti versus LAG-3 antagonist and or to understand how membrane-bound versus soluble LAG-3 function. While the membrane-bound LAG-3 is a negative regulator of T-cell receptors similar to PD-1 (blocking LAG-3 and PD-1/PD-L1 can restore human T cell function), soluble LAG-3 (a spliced variant of LAG-3 gene is translated to a soluble form of LAG-3) promotes Immune activity via MHC class II binding and activation of T-cells.

The soluble form (sLAG-3):

- enhanced maturation of monocyte-derived dendritic cells in vitro
- induced antigen-specific CD4 or CD8 cells producing IL-2, IFN $\gamma$ , or TNF- $\alpha$  as detected by intracellular staining.

## Immutep's Clinical Programs

1) AIPAC - Active immunotherapy PAClitaxel in ER-Positive, HER2-Negative Breast Cancer

1) A study in hormone receptor-positive metastatic breast carcinoma patients to test a new schedule of efti (IMP321, eftilagimod alpha) as adjunctive to a weekly treatment regimen of paclitaxel (AIPAC-002) – Phase 1 - NCT04252768

### Study Design

Study Type ⓘ : Interventional (Clinical Trial)  
 Estimated Enrollment ⓘ : 24 participants  
 Allocation: N/A  
 Intervention Model: Single Group Assignment  
 Masking: None (Open Label)  
 Primary Purpose: Treatment  
 Official Title: **AIPAC-002** (Active Immunotherapy PAClitaxel-002):  
 Metastatic Breast Carcinoma Patients  
 Estimated Study Start Date ⓘ : June 2021  
 Estimated Primary Completion Date ⓘ : June 2022  
 Estimated Study Completion Date ⓘ : February 2023

Source: [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

This is a multicenter, multinational Phase Ib study in female HR+ MBC patients who did not receive Her2-targeted therapy. Treatment consists of a chemo-immunotherapy phase followed by a maintenance phase. The chemo-immunotherapy phase consists of 4 weeks of 6 cycles. During each cycle, the subject will receive 80 mg/m<sup>2</sup> paclitaxel intravenously on Day 1, 8, and 15 and 30 mg efti subcutaneously on Day 1 and 15 in a 28-day (4-week) cycle. Efti will always be given after paclitaxel. The maintenance phase comprises 6 visits with 4 weekly intervals; during each visit, 30 mg efti is given subcutaneously as monotherapy. A total of 24 subjects will be enrolled in the study. The primary goal of the AIPAC-002 study is the safety and tolerability profile of efti in combination with weekly paclitaxel both given the same day in contrast to subsequent days as in the AIPAC trial.

**Primary endpoint:** Safety and tolerability profile of efti in combination with weekly paclitaxel both given the same day (Time Frame: up to 12 months)

2) IMP321 (eftilagimod alpha) as adjunctive to a standard chemotherapy paclitaxel metastatic breast carcinoma – Phase2b - NCT02614833

### Study Design

Study Type ⓘ : Interventional (Clinical Trial)  
 Estimated Enrollment ⓘ : 241 participants  
 Allocation: Randomized  
 Intervention Model: Parallel Assignment  
 Masking: Double (Participant, Investigator)  
 Primary Purpose: Treatment  
 Official Title: **AIPAC** (Active Immunotherapy PAClitaxel)  
 Study Start Date ⓘ : December 2015  
 Actual Primary Completion Date ⓘ : March 2020  
 Estimated Study Completion Date ⓘ : May 2021

Source: [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

This study evaluates efti in combination with paclitaxel, a standard of care chemotherapy, as a chemo-immunotherapy combination. The trial is a randomized, double-blinded, placebo-controlled clinical study with 226 evaluated HR+ metastatic breast cancer patients and is taking place across more than 30 clinical trial sites in Germany, the UK, France, Hungary, Belgium, Poland, and the Netherlands.

**Experimental: Paclitaxel + IMP321:** The chemo-immunotherapy phase consists of 6 cycles of 4 weeks. The patient will receive weekly paclitaxel at Days 1, 8, and 15 with adjunctive treatment of study agent, either IMP321, on Days 2 and 16 of each 4-week cycle. After completion of the 6-cycle chemo-immunotherapy phase, responding or stable patients will receive a study agent (IMP321) every 4 weeks during the maintenance phase for an additional period of up to 12 injections.

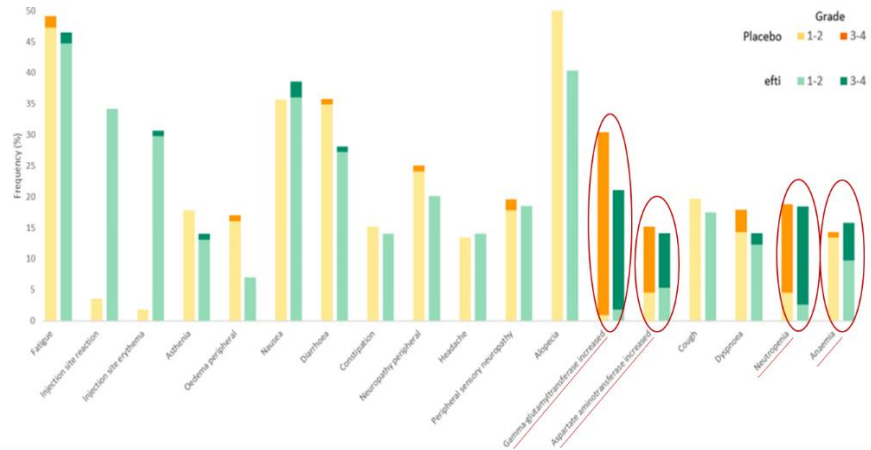
**Active Comparator: Comparator: Paclitaxel + Placebo**

The chemo-immunotherapy phase consists of 6 cycles of 4 weeks. The patient will receive weekly paclitaxel at Days 1, 8, and 15 with adjunctive treatment of study agent, placebo, on Days 2 and 16 of each 4-week cycle. After completion of the 6-cycle chemo-immunotherapy phase, responding or stable patients will receive a study agent (placebo) every 4 weeks during the maintenance phase for an additional period of up to 12 injections.

**Primary endpoint:** i) Stage 1 to determine the recommended phase two dose for the randomized phase (Time Frame: Up to 12 months), ii) Assessment of Progression-Free Survival (PFS) (Time Frame: Up to 37 months)

**Based on data presented at the 2020 San Antonio Breast Cancer Symposium (SABCS) from the AIPAC Phase 2b study,** treatment-related adverse events (AEs) were seen in almost every patient for both paclitaxel+placebo (n=114) and paclitaxel+efti (n=112) arms (100% vs. 99% respectively). 2 patients died in the treatment arm, while 3 patients died in the placebo arm. 5.3% of the patients discontinued treatment in pacli+efti arm in comparison to 6.3% in pacli+placebo arm. Most frequent grade 3-4 AEs were a gamma-glutamyltransferase increase, aspartate aminotransferase increase, neutropenia, and anemia. Unlike placebo arm, efti caused injection site erythema and reaction at grade 1-2 level.

**Exhibit 10. AIPAC Phase 2b clinical results safety - Most common (≥15%) TEAEs in any arm**

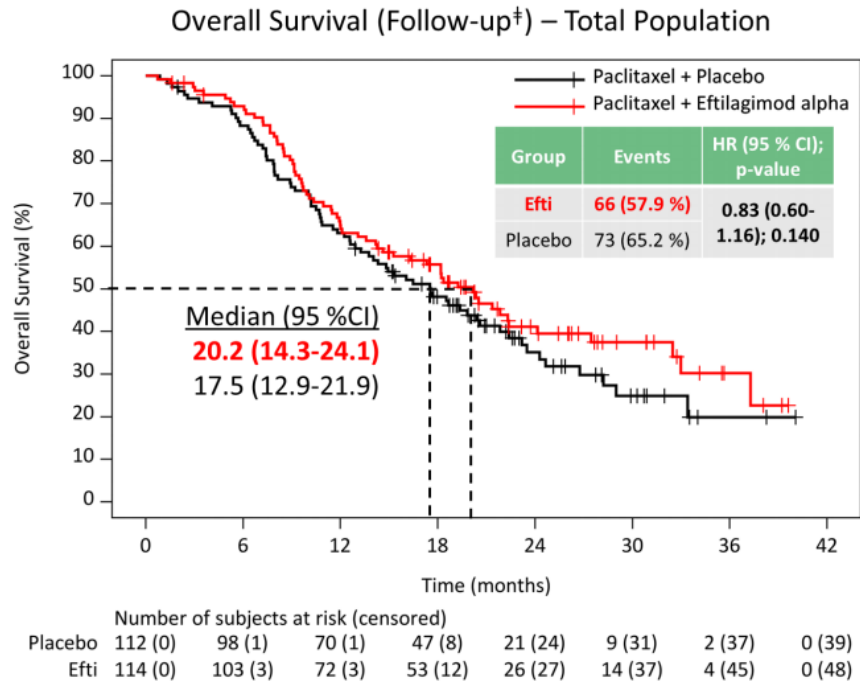


Summary of treatment-emergent adverse events (TEAEs) <sup>¶</sup>	Paclitaxel + efi N=114, n (%)	Paclitaxel + Placebo N=112, n (%)
≥1 TEAE	113 (99.1)	112 (100)
≥1 TEAE leading to death	2 (1.8)	3 (2.7)
≥1 TEAE leading to efi/placebo discontinuation	6 (5.3)	7 (6.3)
≥1 Grade ≥3 TEAE	78 (68.4)	73 (65.2)

Source: Company SEC filings

In this study, efi plus pacli resulted in 2.7 months OS advantage compared to pacli alone in the overall population (ITT, based on 60% events).

**Exhibit 11. Not statistically significant but improving trend with 2.7 months advantage in median OS with efti in the overall population (IIT).**



Source: Company SEC filings

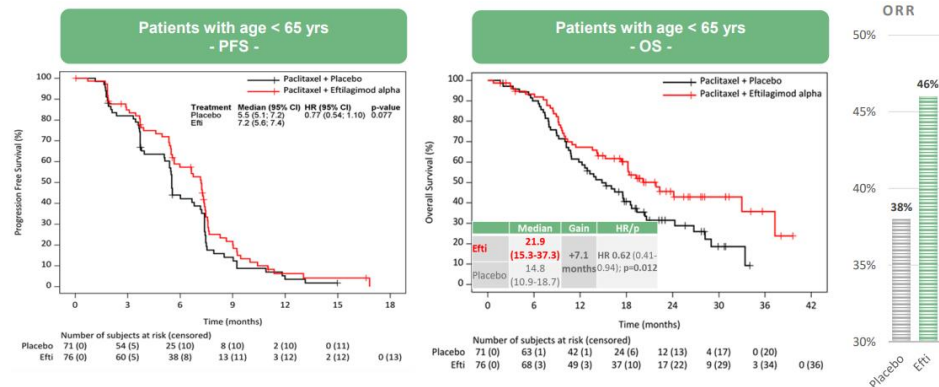
While data represent a positive trend in OS, additional subgroup analysis provided further information:

Subgroup 1: patients < 65 years

- i) Patients younger than 65 did not have statistically significant improvement in the progression-free survival (PFS, median PFS was 5.5 months in placebo arm compared to 7.2 months in efti arm, p=0.077).
- ii) However, statistically significant improvement in overall survival (OS) was observed in patients younger than 65 (median OS 21.9 months in efti versus 14.8 months in placebo arm, p=0.012).
- iii) The overall response rate was 46% with efti compared to 38% on the placebo arm for patients younger than 65.



**Exhibit 12. Efti plus pacli treatment significantly prolonged survival in patients younger than 65 yo but did not significantly improve PFS. The overall response rate was 46% in the efti arm compared to 38% in the placebo arm**

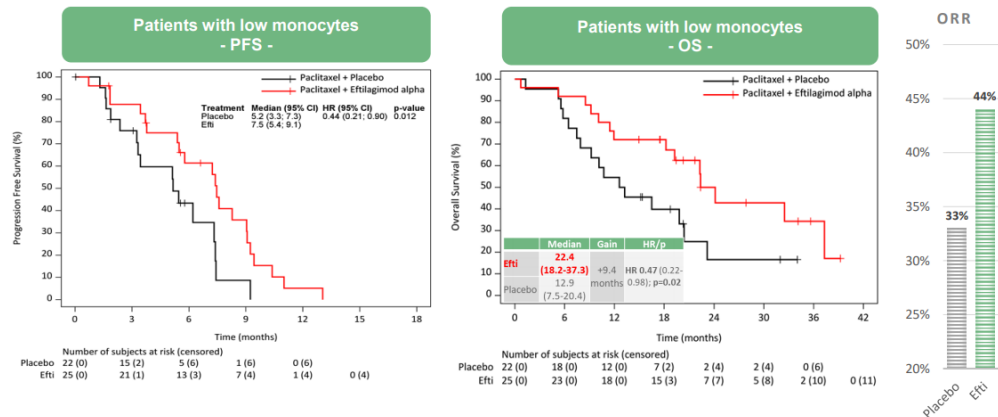


Source: Company SEC filings

Subgroup 2: patients with low monocyte counts

- i) Patients with low monocytes had significant improvement in their median PFS when treated with efti (5.2 months in placebo versus 7.5 months in efti arm, p=0.012).
- ii) Overall survival also increased to 22.4 months for the patients treated with efti compared to 12.9 months for the patients in the placebo arm.

**Exhibit 13. Patients with low monocytes experienced significant OS benefit when treated with efti plus pacli compared to pacli alone**



Source: Company SEC filings

The management states that prior treatment of CDK 4/6 inhibitors has a negative impact on OS in the placebo group (median reduced from 20.0 to 14.9 months), but not in the efti group (median OS 20.9 vs. 20.4 months). As the CDK4/6 agents are now standard and most patients will have received it, this would play favorably for efti.

**What is next?** 2nd OS follow-up analysis planned 2H21.

2) **TACTI-002** Phase 2 TACTI-002 (Two ACTive immunotherapies)

### Study Design

Study Type ⓘ	Interventional (Clinical Trial)
Estimated Enrollment ⓘ	183 participants
Allocation:	Non-Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	<b>TACTI-002</b> (Two ACTive Immunotherapeutics)
Actual Study Start Date ⓘ	February 18, 2019
Estimated Primary Completion Date ⓘ	May 2022
Estimated Study Completion Date ⓘ	May 2023

Source: [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Immutep is evaluating the combination of efti with KEYTRUDA (or pembrolizumab, an anti-PD-1 therapy) in up to 183 patients with 2nd line HNSCC or NSCLC in 1st and 2<sup>nd</sup> line. The study is taking place at 12 clinical sites across Australia, Europe, the UK, and the US and is being conducted in collaboration with Merck. Patients participating in the trial will be given the combination treatment for 12 months using a 30 mg s.c. eftilagimod alpha dosing every 2 or 3 weeks, 200 mg pembrolizumab every 3 weeks.

The primary endpoint is ORR according to iRECIST - time frame: up to 24 months.

### Immutep Presented Data Update From TACTI-002 Study In NSCLC at the 2021 ASCO Annual Meeting

- i) The first data update was from the extension Part A portion of the study that is assessing efti in combination with pembro in 1<sup>st</sup> in NSCLC (unselected for PD-L1) patients. Among 52 patients, 92.3% of the patients had any TEAE, 34.6% of which SAE. The most frequent AEs include asthenia (34.6%), cough (28.8%), dyspnea (28.8%), and others as listed in Exhibit 14. While 52% of the patients experienced grade 3 AE with the most frequent grade 3 AE of dyspnea (13.5%), there were no grade 4 AEs. Five patients died and 6 patients discontinued treatment.

#### Exhibit 14. TACTI-002 Phase 2 Clinical Results Safety - Most common ( $\geq 15\%$ ) TEAEs and general overview of AEs

Adverse event by PT	Any grade N (%)	Grade 3 N (%)	Grade 4/5 N (%)
Asthenia	18 (34.6)	2 (3.8)	-
Cough	15 (28.8)	1 (1.9)	-
Dyspnoea	15 (28.8)	7 (13.5)	-
Decreased appetite	13 (25.0)	1 (1.9)	-
Fatigue	12 (23.2)	-	-
Diarrhoea	11 (21.2)	1 (1.9)	-
Pruritus	11 (21.2)	-	-
Constipation	10 (19.2)	-	-
Anaemia	10 (19.2)	2 (3.8)	-
Back pain	8 (15.4)	2 (3.8)	-
Nausea	8 (15.4)	-	-

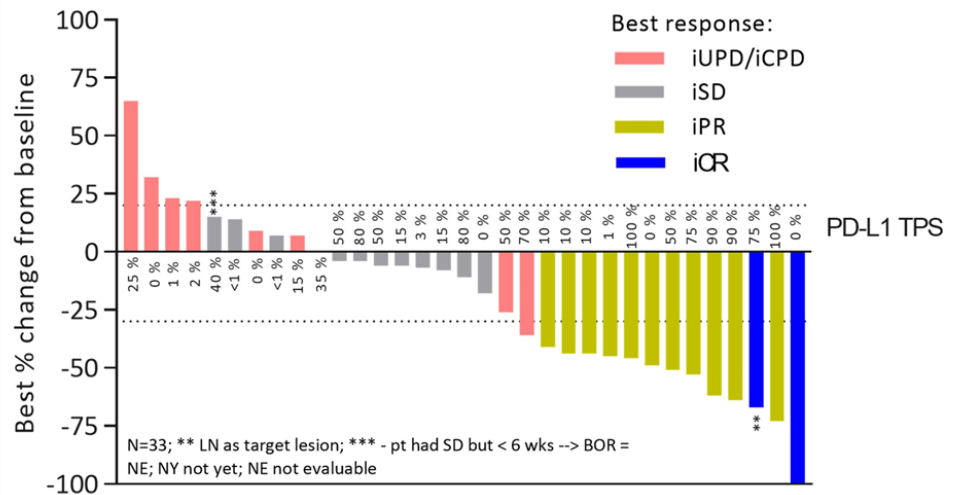
Safety parameter	N (%)
Patients with any TEAE	48 (92.3)
Patients with any SAE	18 (34.6)
thereof related to efti/pembro	3 (5.8) / 3 (5.8)
Patients with any grade $\geq 3$ TEAE	27 (51.9)
thereof related to efti/pembro	4 (7.7) / 5 (9.6)
Patients with fatal TEAEs	5 (9.6)
thereof related to efti /pembro	0
Patients with TEAEs leading to discontinuation of any study treatment	6 (11.5)
thereof related to efti /pembro	3 (5.8) / 2 (3.8)

\* - Safety is displayed for all patients (n=52) recruited who received  $\geq 1$  treatment

Source: Company SEC filings

Among 36 patients, 32 of them were evaluable. Two patients (5.6%) had complete response (CR) 11 patients (30.6%) had partial response, accounting for 36.1% of the overall response rate (ORR). Eleven patients (30.6%) had stable diseases leading to 66.7% diseases control rate (DCR).

Exhibit 15. TACTI-002 Phase 2 NSCLC data



Best overall response, iRECIST	Local Read (investigator) N (%)	Blinded Read (BICR) N (%)
Complete Response	2 (5.6)	2 (5.6)
Partial Response	11 (30.6)	13 (36.1)
Stable Disease	11 (30.6)	10 (27.8)
Progression	8 (22.2)	6 (16.7)
Not evaluable**	4 (11.1)	5 (13.9)
Disease Control Rate	24 (66.7)	24 (66.7)
<b>Overall Response Rate* [95 % CI interval]</b>	<b>13 (36.1) [20.8-53.8]</b>	<b>15 (41.7) [25.5-59.2]</b>
<b>Overall Response Rate – Evaluable pts*** [95 % CI interval]</b>	<b>13 (40.6) [23.7-59.4]</b>	<b>15 (48.4) [30.1-60.9]</b>

\* - All patients stage 1 and 2 (N=36) with ≥ 1 treatment

\*\* - dropped off prior to first staging or were not evaluable post-baseline for any reason

\*\*\* - Evaluable for efficacy meaning ≥ 1 treatment and ≥ 1 post baseline tumor staging

PD-L1	ORR iRECIST* (%)
≥ 50 % TPS	53.8
< 50 % TPS	31.6
≥ 1 % TPS	44.0

\* according to investigator read, evaluable pts only

PD-L1	Median PFS iRECIST* (months)
Unselected	8.2
≥ 50 % TPS	11.8
< 1 % TPS	4.1

\*\* according to investigator read, minimum follow-up of 8.3 months, all patients stage 1 and 2 with ≥ 1 treatment

Source: Company SEC filings

Tumor Proportion Score (TPS) represents the percentage of viable tumor cells showing partial or complete membrane staining and it is used to determine PD- L1 protein expression. The specimen is considered PD-L1 positive if TPS ≥ 50% of the viable tumor cells exhibit membrane staining at any intensity. The results suggest that there is a stronger response in PD-L1 positive patients (53.8% vs.36.1% of ORR and 11.8 vs. 8.2 months of PFS in PD-L1 positive patients vs. unselected patient population, respectively). Despite this correlation, it is notable that responses were seen at all PD-L1 levels including 1 CR with a TPS of 0%.

- 92% responses confirmed,
- 58% confirmed responses ongoing with 6+ months,
- 42% of confirmed responses progressed after 6.5-13.8 months,
- Median DoR estimated 13+ months.

### Immutep Presented Data Update From TACTI-002 Study in HNSCC at the 2021 ASCO Annual Meeting

- ii) The data update from the extension Part C portion of the study assessing efti in combination with pembro in the 2<sup>nd</sup> line of HNSCC (unselected for PD-L1) patients. In 39 patients, 87.7% of the patients had any TEAE, 46.2% of which SAE. The most frequent AEs include hypothyroidism (20.5%), cough (17.9%), asthenia (14.4%), and others as listed in Exhibit 16. While 61.5% of the patients experienced grade 3 AE with the most frequent grade 3 AE of anemia (10.3%). Seven patients died (2 related to treatment) and 6 patients discontinued treatment (1 related to treatment).

#### Exhibit 16. TACTI-002 Phase 2 clinical results safety - Most common (≥15%) TEAEs and general overview of AEs

Adverse event (PT)	Any grade N (%)	Grade 3 N (%)	Grade 4/5 N (%)
Hypothyroidism	8 (20.5)	1 (2.6)	-
Cough	7 (17.9)	-	-
Asthenia	6 (15.4)	-	-
Fatigue	5 (12.8)	-	-
Anaemia	5 (12.8)	4 (10.3)	-
Diarrhoea	5 (12.8)	-	-
Weight decreased	5 (12.8)	-	-
URTI	4 (10.3)	-	-
Back pain	4 (10.3)	-	-
Pain in extremity	4 (10.3)	2 (5.1)	-

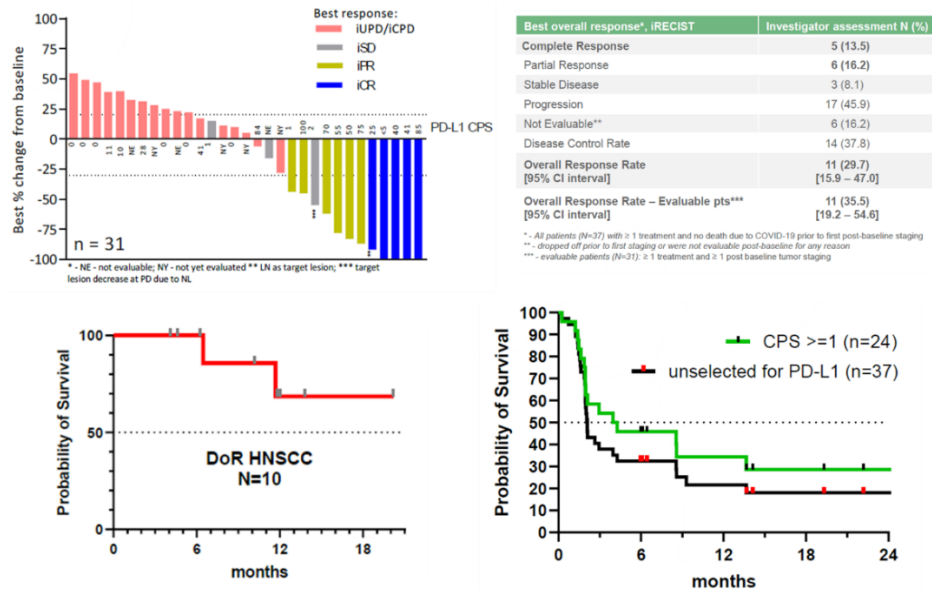
Safety parameter	N (%)
Patients with any TEAE	35 (89.7)
Patients with any SAE	18 (46.2)
thereof related to efti/pembro	2 (5.1) / 2 (5.1)
Patients with any grade ≥3 TEAE	24 (61.5)
thereof related to efti/pembro	4 (10.3) / 3 (7.7)
Patients with fatal TEAEs	7 (17.9)
thereof related to efti/pembro	0 / 0
Patients with TEAEs leading to discontinuation of any study treatment	7 (17.9)
thereof related to efti/pembro	1 (2.6)

\* - Safety is displayed for all patients (N=39) recruited who received ≥1 treatment

Source: Company SEC filings

In 37 HNSCC patients, 31 of them were evaluable. Five patients (13.5%) had complete response (CR); 6 patients (16.2%) had partial response yielding 29.7% overall response rate (ORR). Three patients (8.1%) had stable diseases leading to 37.8% diseases control rate (DCR). 17 patients had progressive disease (45.9% PD).

**Exhibit 17. TACTI-002 2<sup>nd</sup> line HNSCC (Part C) data**



Source: Company SEC filings

In the 2nd line HNSCC, efi plus pembro showed deeper responses with 5 CR. Among selected PD-L1 expression (CPS≥1), median OS (58% events) was 12.6 months, median PFS (71% events) was 4.1 months and ORR was 45.8% (95% CI). Keytruda was approved in 2nd line HNSCC with 16% of ORR rate in 2016 [KEYNOTE 012]. Furthermore, Keytruda was granted approval in the 1st line in 2019 based on the OS benefit in patients (The median OS was 13.0 months for the pembrolizumab plus chemotherapy arm and 10.7 months for the cetuximab plus chemotherapy arm (HR 0.77; 95% CI: 0.63, 0.93; p=0.0067) [KEYNOTE 012].

The next step is the commencement of the TACTI-003 trial in 1<sup>st</sup> line of HNSCC. Immutep is evaluating the combination of efi with KEYTRUDA in up to 154 patients with first line HNSCC. In our view, the current data is promising, TACTI-003 will provide granularity on the positioning of efi in this landscape.

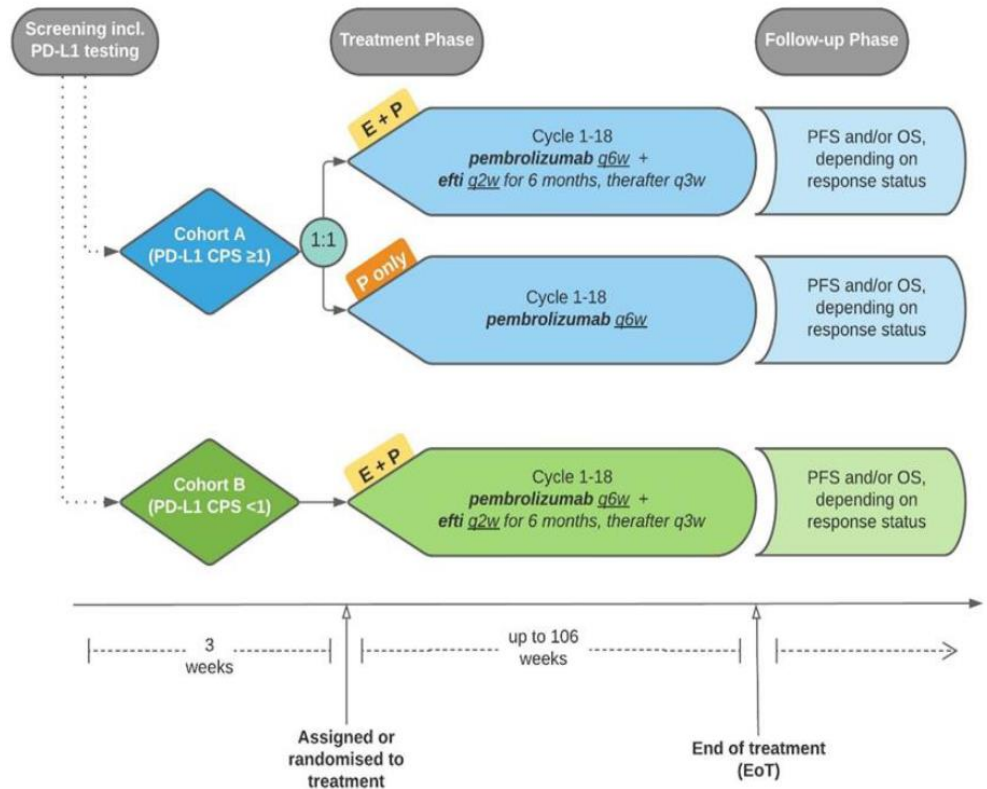
**3) TACTI-003 - Phase 2 TACTI- (Two ACTIVE immunotherapies in 1<sup>st</sup> line HNSCC)**

**Study Design**

Study Type ⓘ	Interventional (Clinical Trial)
Estimated Enrollment ⓘ	154 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	<b>TACTI-003 (Two ACTIVE Immunotherapeutics)</b>
Estimated Study Start Date ⓘ	July 2021
Estimated Primary Completion Date ⓘ	April 2023
Estimated Study Completion Date ⓘ	January 2025

Source: www.clinicaltrials.gov

**Exhibit 18. TACTI-003 Trial in 1<sup>st</sup> line HNSCC current design**



Legend: PD-L1 = programmed cell death ligand 1; CPS= combined positive score; 1 cycle = 6 weeks; q2w = every 2 weeks; q3w = every 3 weeks; q6w = every 6 weeks; E + P = efti + pembrolizumab; P only = pembrolizumab monotherapy

Source: Company SEC filings

In these randomized trials, approximately 154 patients will be enrolled. Patients with high PD-L1 (CPS≥1) expressing patients will either receive pembro alone or pembro in combination with efti, while low PD-L1 (CPS<1) expressing patients will only receive efti - pembro combo.

**Other Trials**

**4) TACTI-mel - Phase 1 TACTI-mel (Two ACTIVE immunotherapies in melanoma)**

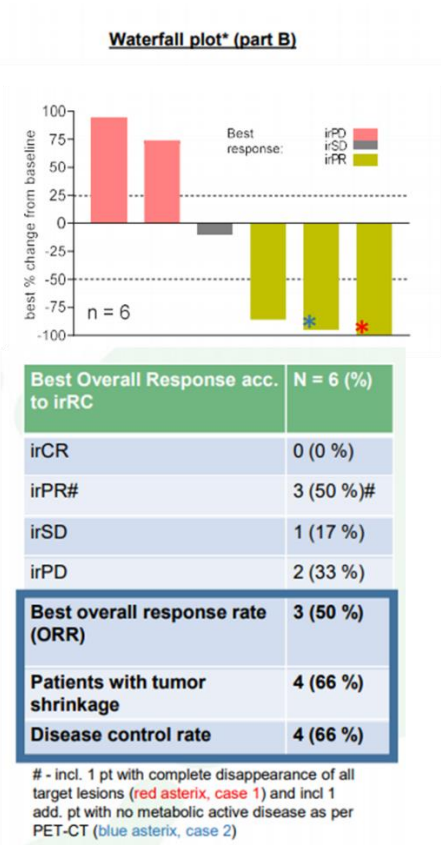
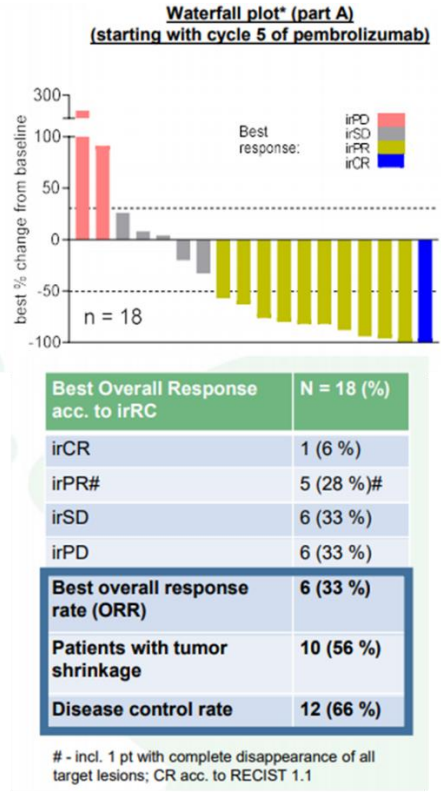
Study Type ⓘ : Interventional (Clinical Trial)  
 Actual Enrollment ⓘ : 24 participants  
 Intervention Model: Sequential Assignment  
 Masking: None (Open Label)  
 Primary Purpose: Treatment  
 Actual Study Start Date ⓘ : April 2016  
 Actual Primary Completion Date ⓘ : August 2019  
 Actual Study Completion Date ⓘ : December 2019

Source: www.clinicaltrials.gov

Immutep’s Phase I clinical trial evaluating efti with KEYTRUDA in 24 patients with unresectable or metastatic melanoma that have had either a suboptimal response or had disease progression with pembrolizumab monotherapy. TACTI-mel is a multi-center, open-label clinical trial involving four cohorts of six patients per cohort.

- i) Part A: 1, 6 and 30 mg efti s.c. every 2 weeks starting with cycle 5 of pembrolizumab
- ii) Part B: efti at 30 mg s.c. every 2 weeks starting with cycle 1 of pembrolizumab

**Exhibit 19. TACTI-mel results in melanoma patients**



Source: Company SEC filings

ORR was 33% in 18 melanoma patients in Part A and 50% in 6 Part B patients. The most common AE was rash, followed by nausea and injection site reaction that was seen in 50%, 29%, and 25% of Part A and B patients, respectively. The results also determined that 30 mg of efti was the recommended dosage level for the Phase 2 trial. This dosage level is currently being used in the ongoing TACTI-002 Phase 2 trial.

**5) Phase 1 YNP01 and YCP02 trials in collaboration with CYTLIMIC**

CYTLIMIC’s cancer peptide vaccine, called CYT001, in combination with efti is evaluated in patients with advanced or metastatic solid cancer. The cancer vaccine is comprised of the combination immunotherapy of an HSP70 derived peptide, a GPC3 derived peptide, Immutep’s IMP321 (efti), and Hiltonol.

CYTLIMIC reported positive results from its YNP01 Phase I clinical trial of CYT001 in early 2020, showing that approximately 70% of patients showed an Immune response to each



peptide. The results were published in the scientific peer-reviewed journal, Cancer immunology, immunotherapy.

#### **6) The INSIGHT-004 (Phase I) with IKF**

INSIGHT is a Phase I study is being conducted by Immutep's partner and trial sponsor, IKF (in Germany) The trial's 4<sup>th</sup> arm, so-called INSIGHT-004, is assessing avelumab alone or in combination with ehti in advanced solid tumors. In 3 cohorts assessing ehti dose escalation in 12 patients, 5 patients showed partial response. One grade 5 AE was observed diffuse myocardial fibrosis.

#### **7) IMP321 - Phase 1 with Chinese partner EOC Pharma**

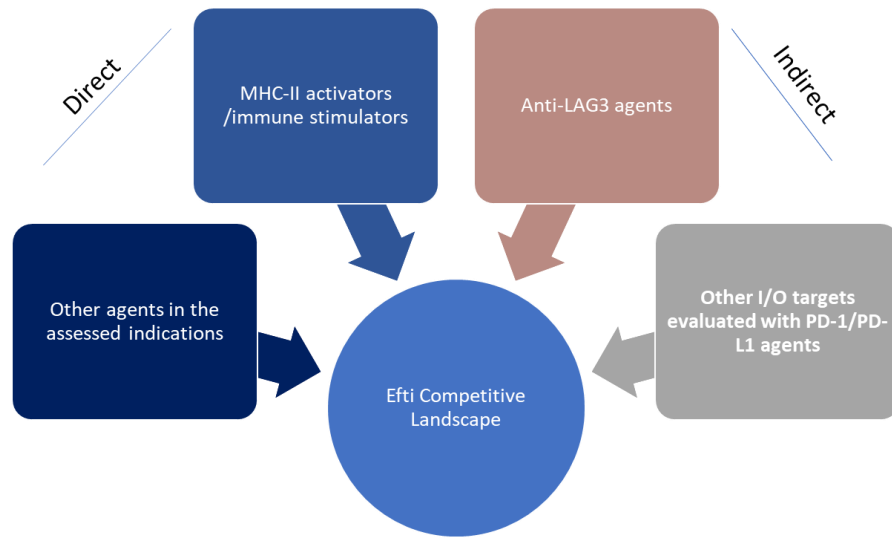
In March 2020 EOC Pharma completed patient recruitment for its ongoing Phase 1 EOC202A1101 study assessing ehti (designated as EOC202 in China) in patients with metastatic breast cancer in China. The results from the trial are expected to be reported in FY 2021 and the company intends to continue advancing ehti following its analysis of the PFS data.

#### **What Does All This Mean?**

As we recognize the Immune mechanism, LAG-3 biology, and function are remarkably complex, the competitive landscape of ehti is multiplex. We see multiple direct and indirect competitors for ehti in clinical development. Although we get into greater detail in the LAG-3 landscape due to recent compelling results, in our view, LAG-3 antagonists do not represent direct competition for Immutep's ehti. While ehti can block LAG-3 in high concentrations, under the current circumstances, ehti acts as an MHC-II activator. Hence, we view four subcategories of competitors for ehti:

- i. Other agents that are currently in clinical development for the assessed indications (HNSCC, NSCLC, mBC)
- ii. MHC-II activators or DC activators that are currently in the clinic (TLR agonist, STING agonist)
- iii. Other I/O agents that are evaluated in combination with PD-1/PD-L1 agents (oncolytic viruses, vaccines, targeted agents)
- iv. LAG-3 agents (antagonist) in clinical development (e.g., relatlimab)

**Exhibit 20. Multiple layers of the competitive landscape for efti**



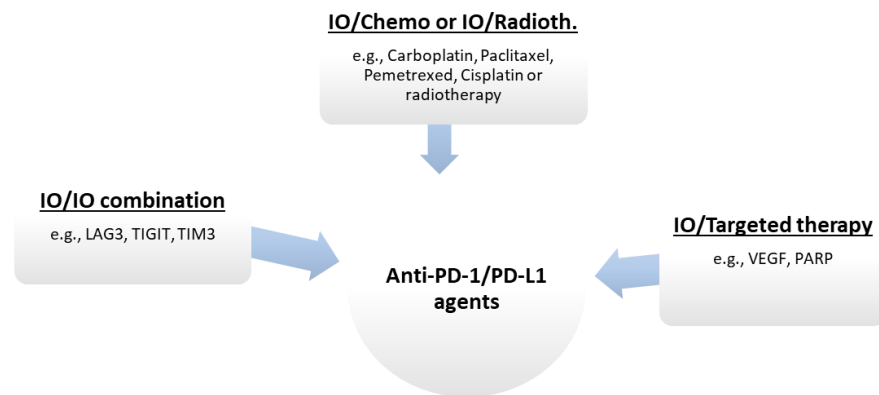
Source: Ladenburg Thalmann research

**1. In the LAG-3 Landscape:**

Checkpoint inhibitor landscape has been the most active space in oncology in the last five years with remarkable clinical activity and numerous approvals across a range of cancers. However, multiple aspects require improvement:

- i) some cancer types (cold tumors) remain to be unresponsive,
- ii) among the patients who respond to treatment, 50% develop resistance,
- iii) a clear predictor (biomarker) for responders or non-responders.

**Exhibit 21. PD-1/PD-L1 combination strategies**



Source: Ladenburg Thalmann research

There are currently 3 main combination strategies including IO/IO combination, IO/chemo or IO/radiotherapy, and IO/targeted therapy to improve the clinical benefit of PD-1/PD-L1 agents. To date, the best response rates were obtained with the ipi+nivo (IO-IO) combination. However, this combination had not been used widely attributed to

unfavorable toxicity profile. LAG-3 is another promising Immune checkpoint target with many players.

## Exhibit 22. LAG-3 competitive landscape

Product	Company		Combination		Stage
Relatlimab	BMS	mAB	PD-1/PD-L1 agent	Melanoma	Phase 3
Eftilagimod	Immutep		PD-1/PD-L1 agent	NSCLC, HNSCC, Melanoma	Phase 2
Fianlimab (REGN3767)	Regeneron	mAB	PD-1/PD-L1 agent	Cancer - Melanoma	Phase 1
Favezelimab (MK-4280)	Merck	mAB	PD-1/PD-L1 agent +/- chemo	Solid tumors	Phase 1/2
IBI110	Innovent Biologics	mAB	w/o PD-1/PD-L1 agent	Advanced Malignancies	Phase 1a/b
LBL-007	Leads Biolabs	mAB	PD-1/PD-L1 agent	Melanoma	Phase 1
INCAGN02385	Agenus/Incyte	mAB	PD-1/PD-L1 agent	Melanoma	Phase 1/2
BI 754111	Boehringer Ingelheim	mAB	PD-1/PD-L1 agent	Solid tumors	Phase 1
Sym022	Symphogen	mAB	PD-1/PD-L1 agent	Cancer	Phase 1
TSR-033	Glaxosmithkline/Anapty	mAB	PD-1/PD-L1 agent	Solid tumors	Phase 1
Tebotelimab	Macrogenics	Bispecific - PD-1xLAG3		DLBCL, HNSCC	Phase 2
F5118	F-star Therapeutics	Bispecific - PD-L1xLAG3		Advanced Malignancies	Phase 1
XmAb22841	Xencor	Bispecific - PD-1xCTLA-4		Selected solid tumors	Phase 1
RG6139	Roche	Bispecific - PD-1xLAG3		Solid tumors	Phase 1
PRS-332	Pieris-Servier	Bispecific - PD-1xLAG3		N/A	Preclinical
YBL-011	Y-Biologics	mAB		N/A	Preclinical

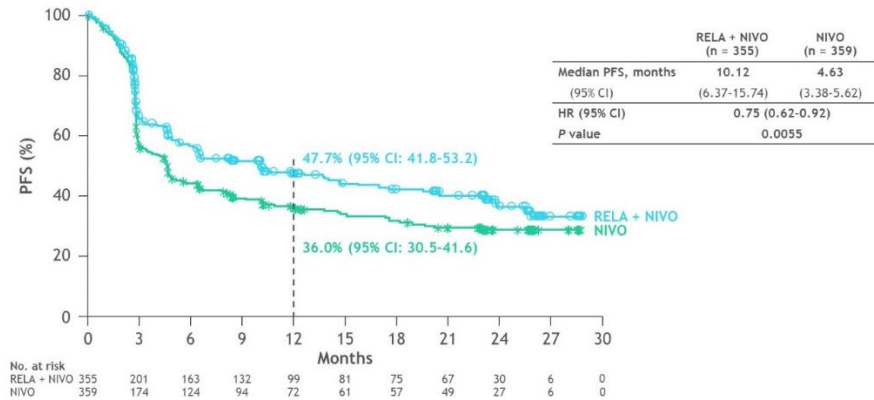
*Note: The mentioned companies are not covered by Ladenburg Thalmann & Co Inc. Mention of specific companies not covered by Ladenburg Thalmann & Co Inc. is not a recommendation to buy, hold or sell the securities mentioned.*

*Source: Company SEC filings and Ladenburg Thalmann research*

**Multiple late-stage LAG-3 targeting programs reported favorable results at ASCO 2021.** While it is significant for the LAG-3 space, it is noteworthy to mention that BMS' data does not validate efti as it has a different mode of action (LAG-3 antagonist vs. LAG-3 agonist/MHC-II activator, respectively).

There late-stage LAG-3 targeting companies presented data at ASCO 2021 including BMS, Regeneron, and Immutep. In the pivotal RELATIVITY-047 study assessing anti-LAG-3/PD-1 combination therapy in 714 first-line melanoma patients, the primary endpoint was met. The results showed superior PFS for relatlimab (rela)+ nivo versus nivo alone, mPFS 10.1 mos vs. 4.63 mos (P=0.0055), respectively. Grade 3/4 drug-related adverse events were 18.9% in the combination arm compared to 9.7% in the Opdivo arm. Drug-related adverse events leading to discontinuation occurred in 14.6% of the patients in the combination arm compared to 6.7% in the Opdivo arm.

**Exhibit 23. Pivotal RELATIVITY-047 study met its primary endpoint: Relatlimab+ nivolumab significantly increased mPFS compared to nivolumab**



CI, confidence interval; HR, hazard ratio. All randomized patients. Statistical model for HR and P value: stratified Cox proportional hazard model and stratified log-rank test. Stratified by LAG-3 (≥ 1% vs < 1%), BRAF (mutation positive vs mutation wild-type), AJCC M stage (M0/M1any[0] vs M1any[1]). PD-L1 was removed from stratification because it led to subgroups with < 10 patients.

12

Source: BMS ASCO presentation

Regeneron’s fianlimab, an anti-LAG-3 monoclonal antibody, in combination with Libtayo was assessed in 33 PD-1 inhibitor naïve advanced melanoma patients. The objective response rate (ORR) of 66.7% exceeding the ORR of 58% seen with Opdivo + Yervoy in the CheckMate-067 study. On the safety front, fianlimab + Libtayo combination had a 27.1% of grade ≥3 treatment-emergent AEs (TEAEs) and 56.3%, 10.5% patients discontinued treatment related to AEs. The toxicity profile of fianlimab presented unfavorably compared to relatlimab.

**Exhibit 24. Phase 1 study assessing fianlimab + cemiplimab achieved 66.7% ORR**

Table 2. Tumor response to fianlimab + cemiplimab		
	Anti-PD-1/PD-L1-naïve (n=33)	Anti-PD-1/PD-L1 experienced (n=15)
ORR, % (95% CI)	66.7 (48.2–82.0)	13.3 (1.7–40.5)
Complete response, n (%)	3 (9.1)	0
Partial response, n (%)	19 (57.6)	2 (13.3)
Stable disease, n (%)	3 (9.1)	4 (26.7)
Progressive disease, n (%)	6 (18.2)	8 (53.3)
NE, n (%)	2 (6.1)	1 (6.7)
DCR, n (%)	25 (75.8)	6 (40.0)
Median PFS, months (95% CI)	NR (4.2, NE)	1.4 (1.3, 10.7)

Reported response rates were by investigator assessment using RECIST 1.1 criteria.  
NE, not evaluable; NR, not reached.

Source: Regeneron ASCO presentation

Beyond these programs, there are multiple other LAG-3 programs in the clinic including:

- 1) Novartis’ LAG525 monoclonal antibody (mAb) -partnered with Immutep- is tested in combination with Spartalizumab (PD-1 mAb) in cancer. The Phase 2 study in NSCLC (n=42), melanoma (n=42), RCC (n=38), mesothelioma (n=57), or TNBC (n=56) patients showed benefit in median progression-free survival (mPFS) in months (90% CI) 3.9 (1.7–5.6) for NSCLC, 2.2 (1.6–5.6) for melanoma, 4.4 (2.1–11.1) for RCC, 5.5 (3.5–6.4) for mesothelioma, and 1.9 (1.6–2.6) for TNBC. ORR response rates were as listed in Exhibit 25 as presented at SITC 2020.

**Exhibit 25. Phase 2 (NCT02460224) LAG525 + spartalizumab (PD-1) study ORR and DCR results: RCC had the highest ORR in PD-1/PD-L1 naïve patients (26.3%)**

ORR, % (90% CI)					
Anti-PD-1/ PD-L1	NSCLC	Melanoma	RCC	Mesothelioma	TNBC
Naïve	n=20 15% (4.2–34.4)	n=20 15% (4.2–34.4)	n=19 26.3% (11.0–47.6)	n=41 17.1%* (8.3–29.7)	n=42 9.5% (3.3–20.5)
Pretreated	n=22 0% (0.0–12.7)	n=22 9.1%* (1.6–25.9)	n=19 5.3% (0.3–22.6)	n=16 6.3%† (0.3–26.4)	n=14 0% (0.0–19.3)
DCR, % (90% CI)					
Anti-PD-1/ PD-L1	NSCLC	Melanoma	RCC	Mesothelioma	TNBC
Naïve	n=20 50% (30.2–69.8)	n=20 45% (25.9–65.3)	n=19 63.2% (41.8–81.2)	n=41 65.9% (51.9–78.0)	n=42 28.6% (17.4–42.1)
Pretreated	n=22 50% (31.1–68.9)	n=22 40.9% (23.3–60.5)	n=19 42.1% (23.0–63.2)	n=16 56.3%† (33.3–77.3)	n=14 21.4% (6.1–46.6)

Source: Chia-Chi Lin et al. *J immunother Cancer* 2020;8:A23

Further data is expected in 2021-2022. If compelling, we expect the company to disclose intend to advance this program in the pivotal setting next year.

2) Innovent Biologics' Phase 1 study of IBI110 (anti-LAG-3 monoclonal antibody) as a single agent and in combination with sintilimab reported data from 40 patients with advanced solid tumors at ASCO 2021. The interim results showed that no adverse event (AE) led to discontinuation of IBI110 or sintilimab and no treatment-related death was reported. Three subjects had achieved a partial response with an objective response rate of 16.7% (3/18), as of April 26, 2021.

**Our view:** Following the RELATIVITY-047 pivotal trial (rela+Opdivo) meeting its primary endpoint, LAG-3 became the third validated checkpoint target, after CTLA-4 and PD-1/L1. Based on the recent data presented by BMS, Immutep, and Regeneron, efti + Keytruda seem to have the most favorable safety profile, as the combination showed 17% grade 3/4 TRAE compared to 25% with fian+ Libtayo, 19% with rela+ Opdivo (taking Yervoy+Opdivo combination as a benchmark, 58% grade 3/4 AE rate and 43% discontinuation). While both rela and fian were assessed in 1<sup>st</sup> line melanoma setting, rela showed a more favorable safety profile. Efti combination in the 1<sup>st</sup> line NSCLC showed 42% ORR in all comers. We believe 50% might be a bar to reach for the efti+PD-1 agent combination. Immutep would potentially utilize a preselected patient population via biomarker identification in its future pivotal studies. In our view, Immutep has a notable chance in this crowded and highly competitive LAG-3 arena considering the following three aspects:

- i) the favorable safety profile,
- ii) compelling response rate (that potentially could improve) with preselected patients in the pivotal trials,
- iii) diverse indication assessment and only fusion protein targeting LAG-3,
- iv) room for multiple approvals similar to the PD-1/PD-L1 landscape.

Product	Company	Indication	Line of therapy	# of patients	ORR	PFS (combo vs. placebo)	Grade 3&4 tox	Discont.
Yervoy + Opdivo	BMS	Melanoma	1L	314	58%	11.5 mos	58%	43%
Relatlimab + Opdivo	BMS	Melanoma	1L	355	ND	10.1 mos	19%	15%
Fianlimab + Libtayo	Regeneron	Melanoma	1L	33	64%	ND	25%	11%
Eftilagimod + Keytruda	Immutep	NSCLC	1L	52	42%	ND	17%	12%

Note: Mention of specific companies not covered by Ladenburg Thalmann & Co Inc. is not a recommendation to buy, hold or sell the securities mentioned

The table includes data presentations at ASCO 2021 focusing on LAG-3 as a target, in addition to Yervoy and Opdivo as a benchmark in melanoma. Relatlimab and fianlimab are LAG-3 antagonists, efi is a soluble LAG-3 and/or MHC-II activator. As we previously stated, we think anti-LAG agents do not represent a direct competition or validation to efi unless they are assessed within the same disease landscape.

## 2. In the assessed disease landscapes

### a. Putting things in perspective in the metastatic breast cancer landscape:

Following further data analysis Phase 1b AIPAC study, the company intends to advance efi in the clinic for metastatic breast cancer patients. Approximately 15-20% of metastatic breast cancers are characterized by overexpression or amplification of human epidermal growth factor receptor 2 (HER2). And the recommended first-line therapy for HER2-positive metastatic breast cancer consists of the anti-HER2 monoclonal antibodies trastuzumab and pertuzumab given with a taxane. The CLEOPATRA (Clinical Evaluation of Pertuzumab and Trastuzumab) trial assessed the combination of trastuzumab, pertuzumab, and docetaxel. Based on the results, the median duration of progression-free survival was 18.7 months and overall survival was 56.5 months. Standard second-line therapy is trastuzumab emtansine (the antibody-drug conjugate) that showed an objective response of 43.6% (95% confidence interval [CI], 38.6 to 48.6) and a median duration of progression-free survival of 9.6 months when the drug was administered after trastuzumab and a taxane. Beyond second-line therapy, no uniformly accepted standard of care was defined, and the currently available options have limited benefit, with response rates of approximately 9 to 31% and a duration of progression-free survival ranging from 3 to 6 months.

However, in December 2020, margetuximab-cmkb (marge) in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens. The Phase 3 SOPHIA (NCT02492711) study evaluated margetuximab plus chemotherapy or trastuzumab plus chemotherapy.

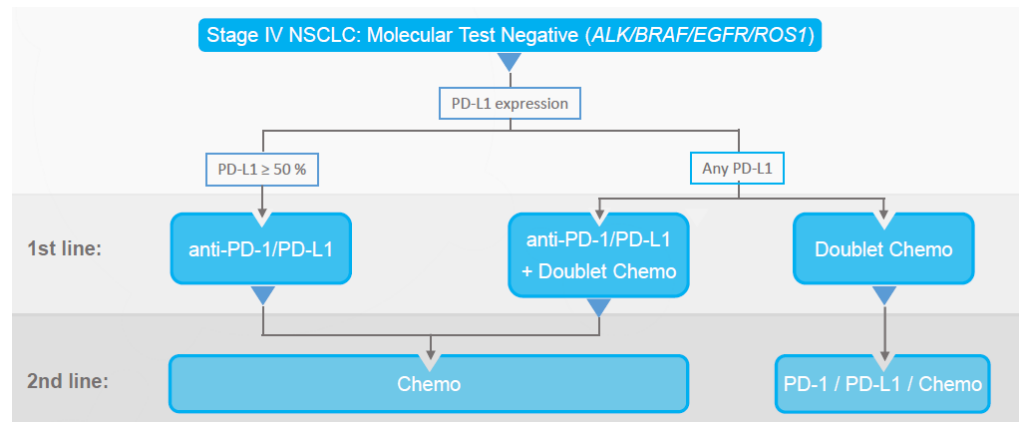
- i. Median PFS in the margetuximab arm was 5.8 months (95% CI: 5.5, 7.0) versus 4.9 months (95% CI: 4.2, 5.6) in the control arm (HR 0.76; 95% CI: 0.59, 0.98; p=0.033),
- ii. confirmed ORR was 22% (95% CI: 17, 27) with a median DOR of 6.1 months (95% CI: 4.1, 9.1) in the margetuximab arm in comparison to an ORR of 16% (95% CI: 12, 20) and median DOR of 6.0 months (95%CI: 4.0, 6.9) in the control arm.

While marga was approved based on mPFS, 7.1-month survival benefit was observed from efiti with chemotherapy for patients under 65 years of age (a median survival benefit of 21.9 months vs. 14.8 months in the placebo group, marking close to a 50% improvement in survival).

#### b. Putting things in perspective in the NSCLC landscape

The metastatic lung cancer market is the most attractive PD1 category accounting for 40% of \$16 billion in 2020 US sales. It is established that anti-PD-1/PD-L1 is the backbone of treatment as monotherapy or in combination with chemotherapy. As it is widely accepted to use PD-1/PD-L1 agents as the backbone of therapy, multiple combination strategies such as IO-IO, IO-chemo, IO-targeted therapy, are evaluated in the clinic to improve the clinical benefit.

#### Exhibit 26. Treatment methodology for 1<sup>st</sup> line NSCLC



Source: Company SEC filings

**Exhibit 27. FDA-approved immunotherapy monotherapy or combination options for first-line therapy**

Monotherapy	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab <sup>1,2</sup>	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS ≥1%	0.63
Atezolizumab <sup>3</sup>	5/18/20	IMpower110	PD-L1 TPS ≥50, EGFR and/or ALK wt	0.59
Cemiplimab <sup>4</sup>	2/22/2021	EMPOWER-Lung 1 (Study 1624)	PD-L1 TPS ≥50, EGFR and/or ALK and/or ROS1 wt	0.57

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab + Platinum and pemetrexed <sup>1</sup>	8/20/18	KEYNOTE-189	Nonsquamous	0.49
Pembrolizumab + Carboplatin, paclitaxel or <i>nab</i> paclitaxel <sup>2</sup>	10/30/18	KEYNOTE-407	Squamous	0.64
Atezolizumab + Carboplatin and paclitaxel and bevacizumab <sup>3</sup>	12/6/18	IMpower150	Nonsquamous	0.78
Atezolizumab + Carboplatin and <i>nab</i> paclitaxel <sup>4</sup>	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab + Ipilimumab <sup>5</sup>	5/15/20	CheckMate-227	PD-L1 TPS ≥1, EGFR and/or ALK wt	0.62
Nivolumab + Ipilimumab and chemotherapy <sup>6</sup>	5/26/20	CheckMate-9LA	EGFR and/or ALK wt	0.69

Source: Company SEC filings, MOASC Summit 2021

Taking ipi+nivo and ipi+nivo+chemo as a benchmark

As shown in Exhibit 27, multiple monotherapy and combinations are available in 1<sup>st</sup> line NSCLC. In 2020, the combination of ipilimumab and nivolumab (ipi+nivo) and ipi+nivo plus chemotherapy were approved in the first-line setting.

Unlike the pivotal trials of CheckMate-227 (ipi+nivo) and CheckMate-9LA (ipi+nivo+chemo), the efi-pembro trial does not have a control arm. The highest responses were highlighted in red for each category. ORR, PFS, and DOR rates for efi-pembro seem to be on the high side. Although we like the trend, lack of control arm, as well as limited patient numbers (31 patients in TACTI versus >400 of patients in Keynote/Checkmate studies), make it challenging to derive strong conclusions.



**Exhibit 28. NSCLC data comparison**

Treatment	KEYNOTE-042		TACTI-002	KEYNOTE-407		CHECKMATE-227		CHECKMATE-9LA	
	Chemo	Pembro	Pembro+Efti	Chemo	Pembro+chemo	Chemo	Nivo+ipi	Chemo	Nivo+ipi+chemo
ORR	27%	27%	42%	35%	58%	30%	36%	25%	38%
PFS	No difference		8.2 mos	4.8 mos	6.4 mos	5.6 mos	5.1 mos	5 mos	6.8 mos
DoR			13 mos +	4.9 mos	7.2 mos	6.2 mos	23.2 mos	5.1 mos	10 mos
mOS	12.2 mos	20 mos		11.3 mos	15.9 mos	14.9 mos	17.1 mos	10.7 mos	14.1 mos

Source: Company SEC filings, FDA labels, and Ladenburg research

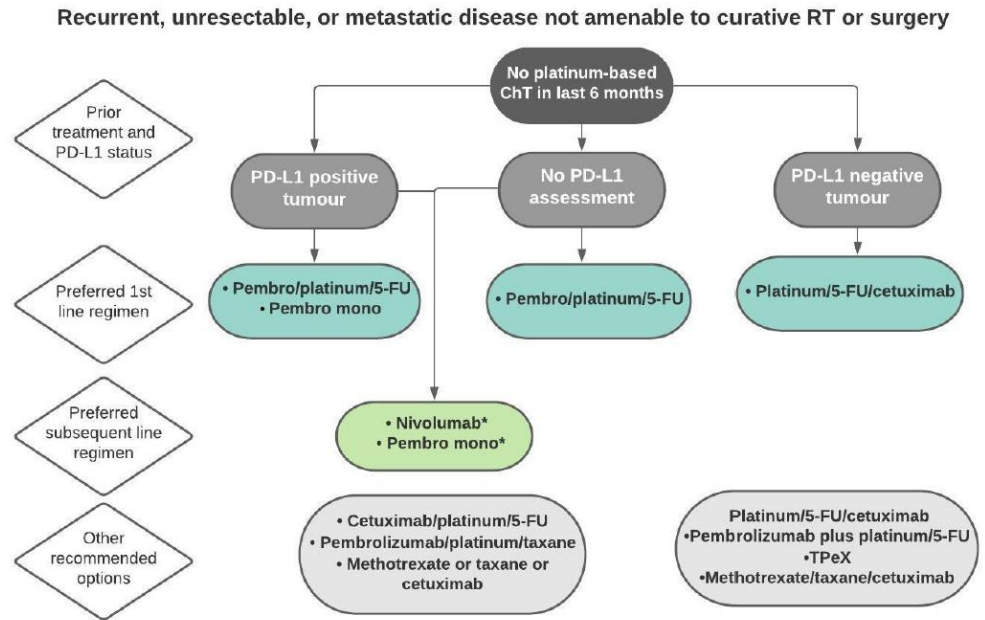
**Recent developments**

The most recent approval was received in February 2021 for Cemiplimab monotherapy in NSCLC with high PD-L1 expression. Based on the results presented at ASCO 2021 from the POSEIDON trial assessing durvalumab and tremimab (PD-L1 and CTLA-4 agents) demonstrated an overall survival benefit in 1<sup>st</sup> line NSCLC.

**c. Putting things in perspective in the HNSCC landscape**

In 2016, nivolumab became the first immunotherapy approved based on Checkmate 141 (NCT02105636) study results. The median survival of the group treated with nivolumab was 7.5 months in comparison to the standard treatment group of 5.1 months (95% confidence interval [CI], P = 0.01). The estimated 1-year survival rates of the nivolumab and standard treatment groups were approximately 36.0% and 16.6%, respectively. The PFS rate of the nivolumab at 6 months was 19.7% compared with 9.9% for the standard treatment group. Nivolumab also leads to fewer severe toxic effects (grade III or IV) than the standard treatment group (13.1% vs 35.1%). In 2019, the pembrolizumab Phase 3 (KEYNOTE 048) trial demonstrated superior OS rates in pembrolizumab combined with chemotherapy group compared with cetuximab combined with chemotherapy (13.0 months vs 10.7 months, P = 0.003). Based on these results, pembrolizumab and chemotherapy became the first-line treatment for patients with recurrent or metastatic HNSCC, whereas pembrolizumab monotherapy is the first-line treatment for patients with relapsed or metastatic PD-L1- positive HNSCC.

**Exhibit 29. Standard of care in HNSCC**



\* pretreated with platinum-based ChT within the last 6 months and immunotherapy-naïve

Sources: NCCN Guidelines Version 1.2021 Head and Neck Cancers  
EHNS-ESMO-ESTRO Clinical Practice Guidelines (2020)

Source: Company SEC filings

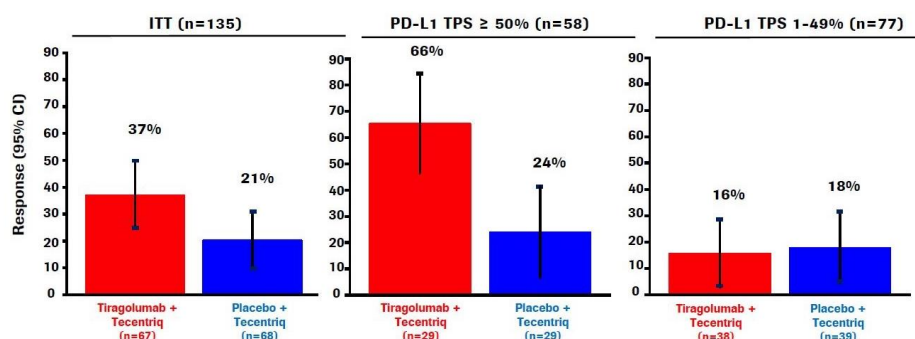
As the company is advancing in the HNSCC landscape and holds a Fast-Track designation, this indication is a significant arena for the company. HNSCC landscape is crowded with multiple I/O agents including (PD-1/PD-L1 agents, CTLA-4, TLR9, STING, CD47) and others. We believe the data from TACTI-003 in the first line of HNSCC will be transformational and provide granularity for the potential positioning of efti in this landscape.

**3. Other PD-1/PD-L1 combinations**

TIGIT is another compelling IO target after LAG-3.

Roche’s tiragolumab plus Tecentriq yielded an ORR of 37% in PD-L1 expressers in comparison to 21% for Tecentriq alone. However, the effect in NSCLC expressing PD-L1 ≥50% was striking: 66% versus, as presented at ASCO 2020.

**Exhibit 30. Cityscape Phase 2 trial tiragolumab (anti-TIGIT) in combination with tecentriq (anti-PD-L1) in 1L NSCLC**



Source: Roche ASCO 2020

Merck’s Esmo dataset with vibostolima combined with Keytruda in checkpoint-naïve demonstrated 46% ORR in PD-L1-expressing NSCLC. However, vibostolima had lackluster activity as monotherapy or combo in checkpoint-refractory patients.

**Exhibit 31. TIGIT targeting is also a crowded landscape with multiple late-stage players**

Industry projects targeting Tigit			
Project	Company	MAb type	Status & enrolment target
Tiragolumab	Roche	IgG1, Fc active	Ph3 (6,567)
Vibostolimab	Merck & Co	IgG1, Fc active	Ph3 (3,090)
Ociperlimab	Beigene	IgG1, Fc active	Ph3 (2,096)
Domvanalimab	Arcus	IgG1, Fc silent	Ph2/3 (917)
BMS-986207	Bristol Myers Squibb	IgG1, Fc silent	Ph1/2 (334)
Etigilimab	Mereo	IgG1, Fc active	Ph1/2 (158)
IBI939	Innovent	?	Ph1 (332)
SGN-TGT	Seagen	IgG1, Fc enhanced	Ph1 (231)
AB308	Arcus	IgG1, Fc active	Ph1 (154)
COM902	Compugen	IgG4, Fc silent	Ph1 (45)
M6223	Merck KGaA	IgG1, Fc active	Ph1 (35)
EOS-448	Iteos	IgG1, Fc active	Ph1 (30)
AGEN1777 (bispecific)	Agenus/Bristol Myers Squibb	Fc enhanced	Preclinical
AGEN1327	Agenus	Fc enhanced	Preclinical

Source: Evaluate Pharma & company presentations.

Note: Ladenburg Thalmann does not cover the above mentioned companies. Mention of specific companies not covered by Ladenburg Thalmann & Co Inc. is not a recommendation to buy, hold or sell the securities mentioned.

**Exhibit 32. Previously unimpressive IO-IO combos**

Project	Company	Mechanism	Setting	Efficacy
ADU-S100	Aduro /Novartis	Sting agonist	Monotherapy	5% ORR (n=40)
TSR-022	Tesaro	Anti-Tim-3	TSR-042 combo	13% ORR (n=31)
MK-7684	Merck & Co	Anti-Tigit	Monotherapy	3% ORR (n=34)
MK-7684	Merck & Co	Anti-Tigit	Keytruda combo	19% ORR (n=43)
MK-4280	Merck & Co	Anti-Lag-3	Monotherapy	6% ORR (n=18)
MK-4280	Merck & Co	Anti-Lag-3	Keytruda combo	27% ORR (n=15)

*Source: SITC.*

*Note: This is not a recommendation to buy, hold or sell the securities for the mentioned companies*

**Other immune stimulators**

To our knowledge, there are no other LAG-3 agonist/MHC II activators; however, there are other immune boosters in the clinic such as STING agonist and TLR agonist. While the 1st generation STING agonists clinical activity was underwhelming (the clinical data from 1st-gen intratumoral STING agonists MK-1454 and ADU-S100 showed lackluster single-agent activity and no clear synergistic efficacy in combo with checkpoint inhibitors), the efforts continue to broaden the clinical activity of STING agonists via i) assessment of 2nd generation cyclic dinucleotide STING agonist (e.g. F-star's SB 11285), ii) using nanoparticle-based therapy (OncoNano Medicine's ONM-501), and iii) coupling it with CAR-T cell therapy J Exp Med (2021) 218 (2): e20200844 that shown compelling synergistic effect in animal models).

TLR9 agonists also had their share of lackluster activity in the clinic. Idera's tilsotolimod in combination with ipilimumab failed to improve ORR in PD-1 refractory, advanced melanoma earlier this year (March 2021). The combination elicited an ORR of 8.8% vs 8.6% with ipilimumab monotherapy and the disease control rates achieved were 34.5% doublet vs 27.2% ipi monotherapy. However, there were also more favorable data from this class of drug candidates. Seven and Eight Biopharmaceuticals' BDB001 (a first-in-class TLR7/8 agonist delivered intravenously) is an immune modulator capable of activating dendritic cells to initiate both innate and adaptive immunity against cancer. BDB001 is assessed in combination with pembrolizumab in advanced solid tumors (NCT03486301). Based on ASCO 2021 presentation, the overall response rate (ORR) was 26%; a disease control rate (DCR) of 58% including 1 CR in 19 solid tumor patients. Clinical responses were seen in subjects with cholangiocarcinoma, hepatocellular carcinoma, melanoma, ovarian carcinoma, and triple-negative breast cancer. SD-101 is an investigational TLR9 agonist from TriSalus Life Sciences. SD-101 is assessed in multiple indications including melanoma, HNSCC. While SD-101 in combination with pembrolizumab (Keytruda) demonstrated early efficacy signals and tolerability in Phase 1b/2 studies for patients with a PD-1 inhibitor-naïve recurrent or metastatic head and neck squamous cell carcinoma (NCT02521870, 22% ORR and 48% DCR), it failed to show significantly improved pCR pembrolizumab in HER2-breast Cancer, presented at ASCO 2021. TLR9 is a highly attractive space with multiple players including Checkmate Pharmaceuticals (CMPI, \$5.1, Not Rated), Excure (XCUR, \$1.8, Not Rated), Miltenyi Biotec (Private), Tallac Therapeutics (Private), and others.

In our view, this class of drug candidates could be viewed as the direct competitors of efi. While there were some underwhelming clinical activities, the efforts continue to broaden the clinical benefit provided by APC activators. Additional data from the studies conducted

with efti or others will be meaningful to derive a conclusion in terms of clinical activity as all these drug candidates including efti are on the way to identify the right i) indication, ii) line of treatment and iii) the combination for a beneficial usage.

## Immutep's Presence Beyond Oncology: Autoimmune Diseases

### LAG-3 targeting in autoimmune disease

LAG-3 is involved in different diseases, including autoimmune diseases, chronic infectious diseases, in addition to cancers. LAG-3 has distinct and complex modes of action driven by its unique structure, isoforms, signaling, and multiple ligands.

Activated T lymphocytes carry major importance in many autoimmune diseases and organ transplant rejection. Depletion of LAG-3+ T cells might lead to targeted immunosuppression that would spare resting T cells but would eliminate pathogenic activated T cells. It was shown that:

- anti-LAG-3 antibodies sharing depleting as well as modulating activities inhibit heart allograft rejection in rats,
- genetic deletion or blockade of LAG-3 exacerbates type 1 diabetes (T1D) in non-obese diabetic (NOD) mice, an animal model of T1D,
- LAG-3-deficient NOD mice demonstrate accelerated infiltration of autoreactive CD4<sup>+</sup> and CD8<sup>+</sup> T cells in islets compared with that in the age-matched LAG-3-sufficient NOD mice,
- NOD mice lacking the cell surface expression of LAG-3 on T<sub>reg</sub> cells exhibit delayed onset and decreased incidence of T1D, which is attributed to the enhanced proliferation and function of T<sub>reg</sub> cells in the absence of LAG-3,
- mice with compound deficiency of LAG-3 and PD-1 develop lethal autoimmune myocarditis on BALB/c, C57BL/6, and B10.D2 backgrounds, indicating that LAG-3 acts synergistically with PD-1 to prevent autoimmunity,
- LAG-3 deficiency or blockade increased the susceptibility to mercury (Hg)-induced autoimmunity by inhibiting the induction of tolerance to Hg in C57BL/6.H2<sup>s</sup> mice,
- in myelin oligodendrocyte glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE) model, LAG-3 blockade abrogated the anti-inflammatory effect of gut environment-induced intraepithelial MOG-specific CD4<sup>+</sup> T cells,
- the ability of in vitro-generated induced T<sub>reg</sub> (iT<sub>reg</sub>) cells to rescue T<sub>reg</sub>-depleted mice from lethal EAE was dependent on the expression of LAG-3 on the T<sub>reg</sub> cells,
- depletion of pathogen-specific activated LAG-3+ T cells might represent a promising new therapeutic approach in diseases where self-antigens (or alloantigen in the case of transplantation) and activated T cells (e.g. multiple sclerosis, rheumatoid arthritis, psoriasis, different forms of thyroiditis, diabetes type I) are involved,
- a LAG-3 cytotoxic antibody prevents T cell-driven skin inflammation in a preclinical DTH model in non-human primates.

LAG-3 is expressed by activated CD4+ and CD8+ T lymphocytes residing in inflamed secondary lymphoid organs and tissues, it is also up-regulated strongly during inflammation. Based on Glaxo Smith Klein's work testing LAG-3 in delayed-type hypersensitivity in non-human primates, the data suggest that the depletion of LAG-3+ cells have an inhibitory action on T helper type 1 (Th1)-mediated immune responses into the skin after antigen challenge. The hypothesis of this data is eliminating antigen-specific activated T cells into the draining lymph nodes leads to reduced capacities to migrate back into the skin and to induce inflammation. Skin-activated Treg cells, presumably expressing LAG-3, migrate to the lymph nodes during cutaneous immune responses where they inhibit immune responses. Based on this knowledge, it can be speculated eliminating LAG-3-positive cells during an intradermal reaction has two opposite actions:

- i) it could eliminate effector T cells and block inflammation, and
- ii) it could prevent Treg cells from inhibiting immune responses in the draining lymph nodes resulting in a reduction of the inflammation due to the absence of effector cells.

The company has i) a partnership with GSK, which had some disappointing news at the beginning of 2021, and ii) a preclinical stage program.

#### **IMP731 and GSK2831781**

GSK2831781 is a depleting anti-LAG antibody that was derived from IMP731, the licensed product (to GSK in 2010). Both IMP731 and GSK2831781 are designed to deplete potentially pathogenic, recently activated LAG-3 expressing T-cells which are enriched at the disease site in T-cell driven immuno-inflammatory disease. GSK was assessing GSK2831781 in Phase 2 in patients with active ulcerative colitis (UC). However, GSK decided to discontinue Phase 2 UC trial in January 2021 based on interim analysis. The Immutep-GSK partnership remains intact for the time being. Immutep could be eligible to receive up to a total of £54 million in milestone and royalties if GSK2831781 is commercialized.

#### **IMP761**

IMP761 is the first agonist antibody that targets the immune checkpoint LAG-3 for the treatment of autoimmune diseases, such as inflammatory bowel diseases, rheumatoid arthritis, and multiple sclerosis. This program is currently at the preclinical stage.

We like the company is going after a wide range of indications and disease areas (oncology and autoimmune diseases). However, we are not yet including autoimmune disease in our model and this area remains as a potential upside on positive news (data or advancement in the clinic) for the shares.

## Partnerships

### Novartis (NVS, \$92.30, Not Rated)

Novartis is Immutep's partner for the development of LAG525, which is a humanized LAG-3 antagonist antibody derived from its IMP701 antibody. In total, Novartis has five ongoing clinical trials for LAG525 in multiple cancer indications including TNBC. The latest update was presented at SITC 2020. We potentially expect further data update in 2H21 or 2022.

### GlaxoSmithKline (GSK, \$40.20, Not Rated)

GSK was conducting a Phase 2 clinical study evaluating GSK2831781 in 242 ulcerative colitis patients. In January 2021, GSK halted the trial based on the assessment of clinical data conducted by the Data Review Committee. The first patient being dosed in September 2019 triggering a milestone payment of GBP4m (AU\$7.4m). GSK previously evaluated GSK2831781 psoriasis.

### LabCorp (LH, \$297.60, Not Rated)

Immutep and LabCorp entered into a License and Collaboration Agreement in October 2020. The agreement is to support the development of immuno-oncology products or services.

### CYTLIMIC (Private)

Immutep continued to collaborate with CYTLIMIC to prepare for clinical trials evaluating efti as part of a cancer peptide vaccine, called CYT001, in patients with advanced or metastatic solid cancer. The cancer vaccine is comprised of the combination immunotherapy of an HSP70 derived peptide, a GPC3 derived peptide, Immutep's IMP321 (efti), and Hiltonol. CYTLIMIC reported positive results from its YNP01 Phase I clinical trial of CYT001 in early 2020, showing that approximately 70% of patients showed an immune response to each peptide. The results were published in the scientific peer-reviewed journal, Cancer immunology, immunotherapy.

### EOC Pharma (Private)

EOC's decision to conduct the new trial follows encouraging first OS data from Immutep's Phase IIb study, AIPAC (see AIPAC above). EOC Pharma has completed its Phase I EOC202A1101 study of efti in patients with metastatic breast cancer in China. The results from the trial are expected to be reported by EOC Pharma in H1 of the calendar year 2021. EOC Pharma is also progressing the manufacturing scale-up work for its trials (see Efti Manufacturing above). EOC Pharma holds the development and commercialization rights to efti in Greater China.

### IKF

INSIGHT is a Phase I study conducted by Immutep's partner, and trial sponsor, The Institute of Clinical Cancer Research, Krankenhaus Nordwest GmbH in Frankfurt, Germany (IKF), in Germany, evaluating efti in advanced solid cancers. The INSIGHT trial includes a 4th arm, called INSIGHT-004 (see below Merck KGaA & Pfizer – INSIGHT-004). Merck KGaA & Pfizer – INSIGHT-004 - Phase I INSIGHT-004 is a Phase I study being conducted in collaboration with Merck KGaA, Darmstadt, Germany, and Pfizer Inc. It is taking place as an amendment under the existing protocol of INSIGHT (see above IKF) and is sponsored by IKF. The study evaluates the combination of efti with avelumab, a human anti-PD-L1 antibody, in 12 patients with different advanced solid malignancies, primarily with gastrointestinal indications and is the first study of an approved and marketed anti-PD-L1 drug in combination with efti.



## Intellectual Property

The company has a strong IP portfolio including 12 patent families relating to its product candidates and related technologies. Throughout the financial year 2020, Immutep received four new patents. In August 2019, the company received a new patent entitled “LAG-3 dosage regime for use in the treatment of cancer” providing further intellectual property protection for Immutep’s method of treating cancer by the administration of a plurality of doses of a recombinant LAG-3 protein. In May 2020, the company received a new patent entitled “Combined Preparations for the Treatment of Cancer” by the Japanese Patent Office. The company also strengthened its intellectual property protection for its therapeutic antibody, LAG525, which is licensed by Novartis, with two new patents. In 2019, Immutep received a patent for LAG525 entitled “Antibody molecules to LAG-3 and uses thereof” by the Japanese Patent Office and similarly by the European Patent Office. These patents relate to LAG525 and its use in the treatment of cancer and infectious disease.

## Leadership

### Marc Voigt - Chief Executive Officer (CEO)

Marc has more than 20 years of experience in the financial and biotech industry, having joined the Immutep team in 2011 as the General Manager, European Operations based in Berlin, Germany. In May 2012, he became Immutep’s Chief Business Officer and in November 2012 its Chief Financial Officer, as well as continuing to focus on its European operations. Having started his career at the Allianz Group working in pension insurances and funds, he moved to the net. IPO AG, a publicly listed boutique investment bank in Frankfurt where he was focused on IPOs and venture capital investments. Marc then worked for several years as an investment manager for a midsize venture capital fund based in Berlin, specializing in healthcare. He also gained considerable operational experience while serving in different management roles with Revotar Biopharmaceuticals, Caprotec Bioanalytics, and Medical Enzymes AG, where he handled several successful licensing transactions and financing rounds. Since 2001, Marc has been a judge and coach in BPW, Germany’s largest regional start-up initiative.

### Dr. Frédéric Triebel - Chief Scientific Officer & Chief Medical Officer

Frédéric Triebel, MD Ph.D., was the scientific founder of Immutep S.A. (2001) and served as the Scientific and Medical Director at Immutep from 2004. Before starting Immutep S.A., he was Professor in immunology at Paris University. While working at Institut Gustave Roussy (IGR), a large cancer center in Paris, he discovered the LAG-3 gene in 1990 and has continued working on this research program since then, identifying the functions and medical use of this molecule. He headed a research group at IGR while also being involved in the biological follow-up of cancer patients treated in Phase I/II immunotherapy trials. He was Director of an INSERM Unit from 1991 to 1996. First trained as a clinical hematologist, Prof. Triebel holds a Ph.D. in immunology (Paris University) and successfully developed several research programs in immunogenetics and immunotherapy, leading to 144 publications and 16 patents.

### Deanne Miller, Chief Operating Officer, General Counsel & Company Secretary

Ms. Miller has broad commercial experience having held legal, investment banking, regulatory compliance, and tax advisory positions, including, Legal Counsel at RBC Investor Services, Associate Director at Westpac Group, Legal & Compliance Manager at Macquarie Group, Regulatory Compliance Analyst at the Australian Securities and Investment Commission, and Tax Advisor at KPMG. She joined the Company as General Counsel and Company Secretary in October 2012 and was promoted to the role of Chief

Operating Officer in November 2016. She has a Combined Bachelor of Laws (Honours) and Bachelor of Commerce, Accounting, and Finance (double major) from the University of Sydney. She is admitted as a solicitor in NSW and a member of the Law Society of NSW.

### **Christian Mueller - Vice President Strategic Development**

Mr. Mueller, MSc BBA, has worked in the field of clinical development of oncology drugs for more than a decade and joined Immutep in 2016. After completing his Master of Science in Biotechnology at the Technical University Berlin, he joined Medical Enzymes AG where he focused on therapeutic enzymes for the treatment of cancer. He was responsible for all deliverables of clinical phase I and II studies, built up a clinical team, and took over the responsibilities for the strategic clinical development of the lead compound. Since 2012 he has worked with Ganymed Pharmaceuticals AG. in developing ideal monoclonal antibodies in the field of immuno-oncology. He was responsible for the clinical development program of the lead antibody and the setup and management of the clinical team. He completed a multinational randomized phase IIb study with 200+ patients investigating the lead antibody in combination with chemotherapy in patients with advanced metastatic gastric cancer. The study was the core asset of a 1.2 billion USD trade sale deal with Astellas. His efforts in the field of clinical development have led to several publications and patents.

### **Company History and Shareholders Information**

Immutep Limited was incorporated under the laws of the Commonwealth of Australia on May 21, 1987. The principal listing of ordinary shares is the Australian Securities Exchange or ASX. The company filed a registration statement on Form 20-F with respect to the ordinary shares with the U.S. Securities and Exchange Commission, or SEC, which was declared effective on April 12, 2012. The American Depositary Shares, or ADSs, each of which represents 10 ordinary shares, are listed on the NASDAQ Global Market, or NASDAQ, under the symbol "IMMP". The Bank of New York Mellon acts as the depository and registers and delivers the ADS.

In December 2014, the company completed the acquisition of Immutep S.A., a private French company. In November 2017, what was then known as Prima BioMed Ltd, changed its name to Immutep Limited to reflect the new strategic direction and management of the business to focus on the development of its portfolio of LAG-3 based immunotherapy assets.

### **Financials**

The share purchase plan (SPP) was closed on July 19, 2021 with the company receiving total application funds of A\$7,175,720. This is in addition to the A\$60 million two-tranche institutional placement (Placement) (details of which were announced to ASX on 21 June 2021) where the issue of shares under the second tranche of the Placement (representing approximately A\$46.3 million). The company expects that 13.8 new shares issued under the SPP will be issued to eligible shareholders on Friday, 23 July 2021 and holding statements is dispatched as of Tuesday, 3 August 2021. The company has over ~850.92 million ordinary shares, ~A114.03 million (US\$85,73).

The net cash used in G&A activities in the quarter was \$242k that includes \$125k in payment of Non-Executive Director's fees and Executive Director's remuneration. The net cash used in Research and Development activities in the quarter was \$1.74 million. The cash flow used in R&D activities for the 9 months from July 2020 to March 2021 was \$7.0 million decreased from \$16.1 million for the 9 months from July 2019 to March 2020 attributed to the declining AIPAC expenses since patients in the AIPAC Phase 2b clinical trial have completed the treatment and moved into the follow-up phase. The cash used in

R&D activities is expected to increase with the commencement of the new Phase 2b TACTI-003 clinical trial. Total net cash outflows used in operating activities in the quarter were \$3.05 million. The cash and cash equivalent balance as of 31 March 2021 was \$51.7 million compared to a balance of \$54.9 million as of 31 December 2020. Following completion of the Placement, Immutep will have a pro forma cash balance of \$114 mm which extends the cash runway to 4Q23.

## Valuation

We value Immutep using a risk-adjusted discounted cash flow model. The DCF model is risk-adjusted for the probability of success of efiti in clinical development. We used a probability estimate to account for financial, clinical, and regulatory risks. For our revenue estimates, we include HNSCC and mBC markets as the company plans to advance in these two indications. We included PD-1/PD-L1 agents in these indications and assume market penetration in the combination setting. We assigned a 50% probability of success in these indications. The model is based on data compiled by previous industry studies (Clinical Development Success Rates 2006-2015 by Bio (Biotechnology Innovation Organization), BioMedTracker, and Amplion)). Using the Gordon Growth Method, we calculate a terminal value of \$2.01 billion and arrive at our \$8.30 price target.

Total PD-1/PD-L1 sales	2021	2022	2023	2024	2025	2026
<b>HNSCC</b>	\$2,106.60	\$2,697.29	\$3,068.55	\$2,925.43	\$2,665.54	\$2,545.65
<b>mBC</b>	\$ 695.62	\$1,479.24	\$2,192.40	\$3,138.71	\$3,834.34	\$4,232.60

Share Valuation			
	Probability	Adj. Value	Full Value
<b>HNSCC</b>	50%	\$ 5.3	\$ 10.5
<b>mBC</b>	50%	\$ 1.8	\$ 3.5
Cash		\$ 1.3	\$ 1.3
<b>Price Target</b>		<b>\$ 8.3</b>	<b>\$ 15.3</b>

Source: Ladenburg Thalmann research estimates

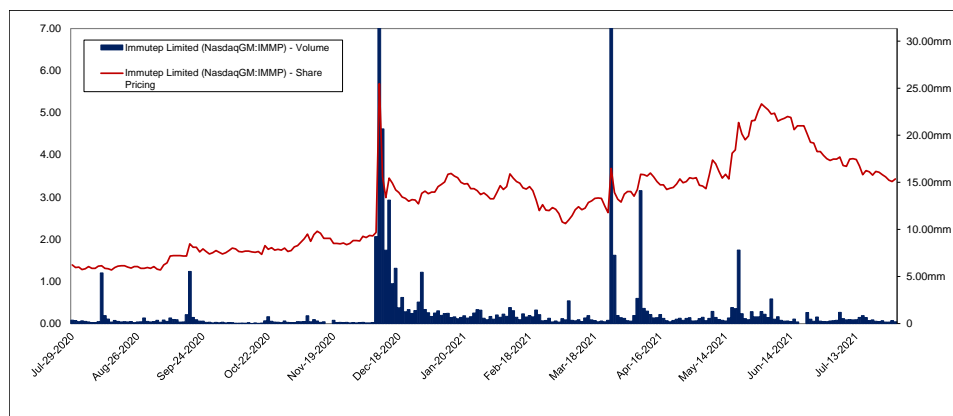
In addition to the DCF model, we have also selected a group of comparable biotechnology companies with a candidate medicine in Phase 1/2 clinical trials for the treatment of cancer. Based on the comparative analysis, Immutep's current EV represents a 70% discount to the peer group. As we note in this report that the efiti's competitors, hence Immutep's peers have multiple layers [i. A similar model of action, ii. Landscape, iii. Market positioning, iv. Combination strategy]. We have eliminated the large pharma competitors. The median EV for the 9 companies is \$797 . We apply a 25% discount to IMMP 's EV to the average EV of the comparable reference companies, which derives an EV of \$597 mm for IMMP. Combining with IMMP's ~\$110M pro forma cash, this gives a ~\$711M market cap valuation for IMMP, or \$8.30 per share. Based on our target, the potential implied return is over 140%.

### Valuation of IMMP through comparable companies

Company Name	Ticker	Market			Cash	Debt	EV	EPS	Earnings Yield (E/P)
		Share Price	Cap (\$ mm)						
Arcus Biosciences, Inc.	RCUS	30.13	2230	390	17	1857	-2.77	-0.09	
Checkmate Pharmaceuticals, Inc.	CMPI	5.20	109	39	0	69	-3.25	-0.63	
Immutep Limited	IMMP	3.46	408	42	8	374	-0.05	-0.01	
iTeos Therapeutics, Inc.	ITOS	24.77	843	321	3	525	-2.12	-0.09	
PDS Biotechnology Corporation	PDSB	11.03	303	25	1	278	-0.70	-0.06	
Vaccinex, Inc.	VCNX	2.46	70	29	3	44	-1.34	-0.54	
ALX Oncology Holdings Inc.	ALXO	60.92	2356	430	1	1927	-2.08	-0.03	
Bolt Biotherapeutics, Inc.	BOLT	11.66	405	95	11	320	-11.00	-0.94	
Dynavax Technologies Corporation	DVAX	9.41	1070	79	217	1208	-0.58	-0.06	
MacroGenics, Inc.	MGNX	25.30	1525	189	28	1364	-2.27	-0.09	
<b>Average EV</b>						<b>797</b>			

Note: Of the companies mentioned Ladenburg Thalmann only covers IMMP. Mention of specific companies is not a recommendation to buy, hold or sell the securities mentioned

Source: Ladenburg Thalmann research and CapIQ; Price as of 8/2/2021



<b>Price</b>	3.52
<b>Market Cap (mm)</b>	408.44
<b>Cash (mm)</b>	54.88
<b>Debt (mm)</b>	9.75
<b>Enterprise Value (mm)</b>	363.31
<b>52-week High, Low</b>	7.95 1.22
<b>Volume (90-day average)</b>	0.04
<b>Float (mm), % Float</b>	726.74 95.38

Analyst Ratings	Count	%
Buy	2	100%
Hold	0	0%
Sell	0	0%
<b>Total</b>	<b>2</b>	<b>100%</b>

Holder Name	Holder % of Shares Outstanding
BNY Mellon Asset Management	36.84
Australian Ethical Investment Ltd.	5.46
Tavistock Life Sciences	2.62
Morgan Stanley, Investment Banking and Brokerage Investments	1.41
Voigt, Marc	1.16
Triebel, Frederic	0.78
Verition Fund Management LLC	0.69
BlackRock, Inc.	0.60
Miller, Deanne	0.39
Turnbull, Lucinda M F Hughes	0.38

Insider Holder	Insider % of Shares Outstanding
Voigt, Marc	1.16
Triebel, Frederic	0.78
Miller, Deanne	0.39
Turnbull, Lucinda M F Hughes	0.38

Note: Past performance is not indicative of future results

Source: Ladenburg Thalmann research and CapIQ; Price as of 7/29/2021

## Investment Risks

IMMP is subjected to many of the risks associated with investing in micro- to mid-cap biotech companies. In our view, the primary risks to an investment in IMMP shares include, but are not limited to:

**Clinical risk.** Although efiti holds a great promise as an APC activator, there is an inherited risk in drug development. Immutep's efiti has shown compelling results in multiple indications such as non-small cell lung cancer, head, and neck cancer; however, it has not yet been tested in a pivotal setting. In addition, none of the current data showed head-to-head comparison to a placebo control arm in the clinical setting. Despite the promise, we recognize further data validation will be key. Thus, similar to the situation with the anti-PD-L1 landscape, it remains to be clinically demonstrated which indication retaining or removing activity is better for the efficacy and safety profile.

**Regulatory risk.** The regulatory approval processes of the agencies (FDA or EMA) are lengthy, time-consuming, and inherently unpredictable. In the case of IMMP not obtaining regulatory approval for product candidates, its business will be materially adversely affected. If IMMP fails to comply with the U.S. or foreign regulatory requirements, regulatory authorities could withhold marketing or commercialization approvals, limit or withdraw any marketing or commercialization approvals the company may receive and subject the company to other penalties that could materially harm their business.

**Competition risk.** IMMP faces many direct and indirect competitions for its lead asset, efiti. There are a large number of companies focusing on the development of APC activators, and also other assets in the indication efiti being evaluated. All cancer indications IMMP is assessing including NSCLC, HNCLC, melanoma, and others, are highly competitive fields. If IMMP's products cannot demonstrate competitive differentiation from competing products, their commercial opportunities could be significantly impaired.

**Financial risk.** As with a majority of development-stage biotechnology companies, the ability to maintain sufficient funding is critical to the progress of pipeline candidates. Should the company experience problems raising sufficient capital, its development programs' progress could be significantly impeded, leading to both delays in development timelines as well as potential negative effects on investor confidence. Each of these could have a negative impact on the share price.

The company has a history of operating losses and may not achieve or maintain profitability in the future.

The company is exposed to significant risks related to ongoing research and development efforts and might not be in a position to successfully develop any product candidate. Any failure to implement the company's business strategy could negatively impact business, financial condition and results of operations.

The company's status as emerging growth company may reduce the amount of information available to investors.

The outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, could adversely impact business, including non-clinical studies and clinical trials.

The company's ordinary shares may be considered a "penny stock" under SEC regulations which could adversely affect market trading in the company's ADSs.

If the company is or becomes a passive foreign investment company (PFIC), then that would subject U.S. investors to adverse tax rules.

Currency fluctuations may adversely affect the price of the ADSs relative to the price of the company's ordinary shares.

Australian takeovers laws may discourage takeover offers being made for the company or may discourage the acquisition of large numbers of the company's shares.

Rights as a holder of ordinary shares are governed by Australian law and Constitution which differ from the rights of shareholders under U.S. law. Holders of the company's ordinary shares or ADSs may have difficulty in effecting service of process in the United States or enforcing judgments obtained in the United States.

The company is exposed to differing legal and tax laws in multiple jurisdictions, including complex transfer pricing rules in Australia.

**Immutep***Key Terminology*

AE	Adverse event
APC	Antigen-presenting cell
chemo	chemotherapy
CI	Confidence interval
CR	Complete Response
efti	Eftilagimod alpha
HNSCC	Head and neck squamous cell carcinoma
iCPD	Confirmed progressive disease
iRECIST	Immune responses assigned using Response Evaluation Criteria in Solid Tumours
iUPD	Unconfirmed progressive disease
LAG-3	Lymphocyte Activating 3
mBC	Metastatic breast cancer
mPFS	Median progression Free Survival
nivo	Nivolumab
NSCLC	Non-small-cell lung carcinoma
ORR	Overall Response Rate
OS	Overall Survival
pacli	Paclitaxel
pembro	Pembrolizumab
PFS	Progression Free Survival
PR	Partial Response
R/M	Recurrent and Metastatic
R/R	Relapsed or Refractory
rela	Relatlimab
s.c.	Subcutaneous
TEAE	Treatment-emergent adverse event
TLR	Toll-like receptors
TPS	Tumor proportion score
WW	Worldwide

**Exhibit 33. Income Statement***(in A\$)*

(in A\$)	FY 2019A	FY 2020A	6-mos FY 2021A	6-mos FY 2021E	FY 2021 E	FY 2022 E
License revenue	139,782	7,486,444	-	-	-	-
Grant and research revenue	5,497,429	6,252,839	2,212,581	2,168,329	4,380,910	5,038,047
Total revenue	5,637,211	13,739,283	2,212,581	2,168,329	4,380,910	5,038,047
COGS						
Research and development	(16,591,201)	(20,395,982)	(8,437,324)	(8,268,578)	(16,705,902)	(16,872,961)
General and administrative	(6,366,161)	(6,335,679)	(3,116,548)	(2,991,886)	(6,108,434)	(6,138,976)
Total operating expenses	(22,957,362)	(26,731,661)	(11,553,872)	(11,260,464)	(22,814,336)	(23,011,937)
Depreciation and amortisation	(1,879,151)	(2,079,639)	(1,052,916)	(1,010,799)	(2,063,715)	
Other (expense) income	458,037	1,404,281	(9,497,656)	(10,447,422)	(19,945,078)	(20,942,331)
Interest income	397,281	199,541	47,752	23,876	71,628	64,465
<b>Net loss before income taxes</b>	<b>(18,343,984)</b>	<b>(13,468,195)</b>	<b>(19,844,111)</b>	<b>(20,526,479)</b>	<b>(40,370,590)</b>	<b>(38,851,756)</b>
Income tax benefit	-	(37)	(35)	(17)	(52)	-
<b>Net loss after income taxes</b>	<b>(18,343,984)</b>	<b>(13,468,232)</b>	<b>(19,844,146)</b>	<b>(20,526,496)</b>	<b>(40,370,642)</b>	<b>(38,851,756)</b>
Other comprehensive income (loses)	558,415	99,957	(620,751)			
Net loss	(17,785,569)	(13,368,275)	(20,464,897)	(20,526,496)	(40,370,642)	(38,851,756)
EPS	(0.05)	(0.03)	(0.03)	(0.02)	(0.05)	(0.05)
Weighted avg shares outstanding	334,930,046	400,980,184	648,725,286	850,925,283	749,825,285	753,574,411
EPS per ADR	(0.53)	(0.33)	(0.32)	(0.24)	(0.54)	(0.52)
Weighted avg ADRs outstanding	33,493,005	40,098,018	64,872,529	85,092,135	74,982,528	75,357,441

Source: Immutep SEC filings and Ladenburg Thalmann research.



# APPENDIX A: IMPORTANT RESEARCH DISCLOSURES

## ANALYST CERTIFICATION

I, Ahu Demir, Ph.D., attest that the views expressed in this research report accurately reflect my personal views about the subject security and issuer. Furthermore, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report, provided, however, that:

The research analyst primarily responsible for the preparation of this research report has or will receive compensation based upon various factors, including the volume of trading at the firm in the subject security, as well as the firm's total revenues, a portion of which is generated by investment banking activities.

Additional information regarding the contents of this publication will be furnished upon request. Please contact Ladenburg Thalmann, Compliance Department, 640 Fifth Avenue, 4th floor, New York, New York 10019 (or call 212-409-2000) for any information regarding current disclosures, and where applicable, relevant price charts, in regard to companies that are the subject of this research report.

## COMPANY BACKGROUND

Immutep is a clinical-stage biotechnology company focused on the development of immune checkpoint LAG-3 (Lymphocyte Activating 3) therapeutics for oncology and autoimmune diseases. The lead asset Eftilagimod Alpha (efti or IMP321) is being assessed in combination with PD-1/PD-L1 agents or chemotherapy in numerous clinical trials in metastatic breast cancer, non-small-cell lung carcinoma (NSCLC), head and neck squamous cell carcinoma, solid tumors, melanoma, and Covid-19 diseases. The second asset IMP761 is at the preclinical stage for autoimmune disease.

## VALUATION METHODOLOGY

We value Immutep using a risk-adjusted discounted cash flow model. The DCF model is risk-adjusted for the probability of success of efti in clinical development. We used a probability estimate to account for financial, clinical, and regulatory risks. For our revenue estimates, we include HNSCC and mBC markets as the company plans to advance in these two indications. We included PD-1/PD-L1 agents in these indications and assume market penetration in the combination setting. We assigned a 50% probability of success in these indications. The model is based on data compiled by previous industry studies (Clinical Development Success Rates 2006-2015 by Bio (Biotechnology Innovation Organization), BioMedTracker, and Amplion). Using the Gordon Growth Method, we calculate a terminal value of \$2.01 billion and arrive at our \$8.30 price target.

## RISKS

IMMU is subjected to many of the risks associated with investing in micro- to mid-cap biotech companies. In our view, the primary risks to an investment in IMMU shares include, but are not limited to:

**Clinical risk.** Although efti holds a great promise as an APC activator, there is an inherited risk in drug development. Immutep's efti has shown compelling results in multiple indications such as non-small cell lung cancer, head, and neck cancer; however, it has not yet been tested in a pivotal setting. In addition, none of the current data showed head-to-head comparison to a placebo control arm in the clinical setting. Despite the promise, we recognize further data validation will be key. Thus, similar to the situation with the anti-PD-L1 landscape, it remains to be clinically demonstrated which indication retaining or removing activity is better for the efficacy and safety profile.

**Regulatory risk.** The regulatory approval processes of the agencies (FDA or EMA) are lengthy, time-consuming, and inherently unpredictable. In the case of IMMU not obtaining regulatory approval for product candidates, its business will be materially adversely affected. If IMMU fails to comply with the U.S. or foreign regulatory requirements, regulatory authorities could withhold marketing or commercialization approvals, limit or withdraw any marketing or commercialization approvals the company may receive and subject the company to other penalties that could materially harm their business.

**Competition risk.** IMMU faces many direct and indirect competitions for its lead asset, efti. There are a large number of companies focusing on the development of APC activators, and also other assets in the indication efti being evaluated. All cancer indications IMMU is assessing including NSCLC, HNCLC, melanoma, and others, are highly competitive fields. If IMMU's products cannot demonstrate competitive differentiation from competing products, their commercial opportunities could be significantly impaired.

**Financial risk.** As with a majority of development-stage biotechnology companies, the ability to maintain sufficient funding is critical to the progress of pipeline candidates. Should the company experience problems raising sufficient capital, its development programs' progress could be significantly impeded, leading to both delays in development timelines as well as potential negative effects on investor confidence. Each of these could have a negative impact on the share price.

## STOCK RATING DEFINITIONS

**Buy:** The stock's return is expected to exceed 12.5% over the next twelve months.

**Neutral:** The stock's return is expected to be plus or minus 12.5% over the next twelve months.

**Sell:** The stock's return is expected to be negative 12.5% or more over the next twelve months.

Investment Ratings are determined by the ranges described above at the time of initiation of coverage, a change in risk, or a change in target price. At other times, the expected returns may fall outside of these ranges because of price movement and/or volatility. Such interim deviations from specified ranges will be permitted but will become subject to review.

## RATINGS DISPERSION AND BANKING RELATIONSHIPS AS OF (August 3, 2021)

Rating	%	IB %
<b>BUY</b>	79.8	62.0
<b>NEUTRAL</b>	20.2	47.2
<b>SELL</b>	0.0	0.0

## COMPANIES UNDER AHU'S COVERAGE

Ayala Pharmaceuticals Inc. (AYLA)

Immutep Ltd. (IMMP)

## COMPANY SPECIFIC DISCLOSURES

Ladenburg Thalmann & Co. Inc. expects to receive compensation for investment banking and/or advisory services from Immutep Ltd. within the next 3 months.

Ladenburg Thalmann & Co. Inc received compensation for investment banking services from Immutep Ltd. within the past 12 months.

Ladenburg Thalmann & Co. Inc had an investment banking relationship with Immutep Ltd. within the last 12 months.

Ladenburg Thalmann & Co Inc. acted in an advisory capacity for Immutep Ltd. in the last 12 months.

## INVESTMENT RATING AND PRICE TARGET HISTORY

Immutep Ltd. Rating History as of 08/02/2021

powered by: BlueMatrix



B=Buy N=Neutral S=Sell D=Drop Coverage I=Initiate NR=Not Rated

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