immutep
LAG-3 IMMUNOTHERAPY

07

# Investor Update

February 2022

**IN THIS ISSUE:**

MARC VOIGT

# Message from the CEO

I hope that this newsletter finds you and your families safe and well.

I am pleased to report that the Immutep team is helping to lead the LAG-3 therapeutic space as we advance the development of exciting cancer and autoimmune therapies aimed at improving patients' lives. We remain fully committed to this space and currently have more LAG-3 programs under development than any other biotech or pharma. In addition, our lead candidate eftilagimod alpha, or "efti", is unique due to its mechanism of action and has no comparators.

Over the past several months, we reached a transformational period in our company's history as we moved ahead with two late-stage trials in the pipeline, of which one has started and one is in a planning process.

Our late-stage study TACTI-003, is being conducted through our second collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada). TACTI-003 is a Phase IIb trial in first line Head and Neck Squamous Cell Carcinoma (HNSCC) that evaluates efti in combination with MSD's KEYTRUDA® (pembrolizumab) as a first line therapy in approximately 154 patients with HNSCC. This is a randomised, controlled clinical study that will take place across Australia, Europe and the U.S. in up to 35 clinical sites. If the results from this Phase IIb trial are sufficiently positive, we expect it to provide us with registration data to submit to the relevant competent authorities. As a reminder, we were granted Fast Track designation for efti to treat first line HNSCC patients by the U.S. FDA in early April 2021. This collaboration and study builds upon the robust data from TACTI-002 that showed this therapeutic combination provided sustained and durable responses in the second line HNSCC setting, which were reported in June at ASCO and in November at SITC.

A Phase III AIPAC study will evaluate the combination of efti and paclitaxel chemotherapy to treat HER2-negative/HR positive metastatic breast cancer patients, subject to regulatory body and other third party interactions. This potential registrational study is based on the positive data announced from our Phase IIb AIPAC study which showed a statistically significant and clinically meaningful improvement in overall survival for patients in three important pre-defined subgroups. For example, patients under 65 years, less affected by the natural immunosenescence of ageing, saw a 7.5 month survival improvement from efti. This reflects a survival benefit of more than 50% compared to those who received chemotherapy on its own. Patients with low monocyte levels in blood saw a 19.6 month survival improvement from efti, reflecting a survival benefit of more than 150% compared to those who received chemotherapy on its own. These results give us confidence efti has the potential to deliver a meaningful clinical improvement for diverse groups of cancer patients.

Both of the late-stage clinical studies for efti are just the tip of our broader development pipeline which includes a total of four candidates being evaluated in approximately 14 clinical trials. Our two other clinical-stage candidates are exclusively licensed worldwide to our pharmaceutical partners, Novartis and GSK. The fourth candidate, IMP761, is in pre-clinical development for autoimmune disease.

As we evaluate our performance and the positioning of our pipeline in the LAG-3 space, we are pleased with the pace at which our programs are moving, and the number of our programs. This has been at least partially assisted by larger pharma companies helping to generate broader attention and validity of the LAG-3 therapeutic space. In mid-2021, Bristol Myers Squibb announced positive results from its Phase III trial of relatlimab, which is a LAG-3 blocking antibody, in first line melanoma. These results confirmed the significance of LAG-3 in regulating the body's immune system to fight cancer. Recently, Bristol Myers Squibb announced the U.S. Food and Drug Administration (FDA) has accepted for priority review the Biologics License Application (BLA) for relatlimab and nivolumab fixed-dose combination to treat unresectable or metastatic melanoma. The FDA assigned a Prescription Drug User Fee Act (PDUFA) goal date of 19 March 2022. Also the EMA is reviewing relatlimab with a potential registration in mid 2022.

We believe Immutep is set to hold a meaningful, long-term position as a leader in the promising LAG-3 therapeutic space. Efti's mechanism of action is unique because it is not a blocking (or antagonist) antibody that acts as a traditional immune checkpoint inhibitor. Instead, efti is a soluble LAG-3 protein that functions as a major histocompatibility complex (MHC) class II agonist and provides the immune system with a broader stimulation. That is, efti binds to MHC class II molecules on antigen presenting cells, which activates the innate immune system and ultimately drives an adaptive immune response to fight cancer. We often use the analogy of "stepping on the gas" to describe efti's mechanism of action. We contrast efti's mechanism of action to the mechanism of a blocking antibody which can be thought of as "lifting the foot off the brake" of the immune system.

Efti's unique mechanism of action gives it several advantages that broaden Immutep's opportunity. For example, efti can be given at lower doses than other LAG-3 therapeutics, because it only needs to bind to a small percentage of MHC II receptors to trigger clinically effective immune system activation. Achieving a desired clinical benefit at lower dose helps to reduce our cost of goods, another appealing trait for potential partners. Importantly, this unique mechanism of action broadens the number of patients who may benefit from an active immunotherapy, not just patients with a "hot tumor" phenotype (where the tumour is infiltrated with activated T cells which attack and kill tumour cells).

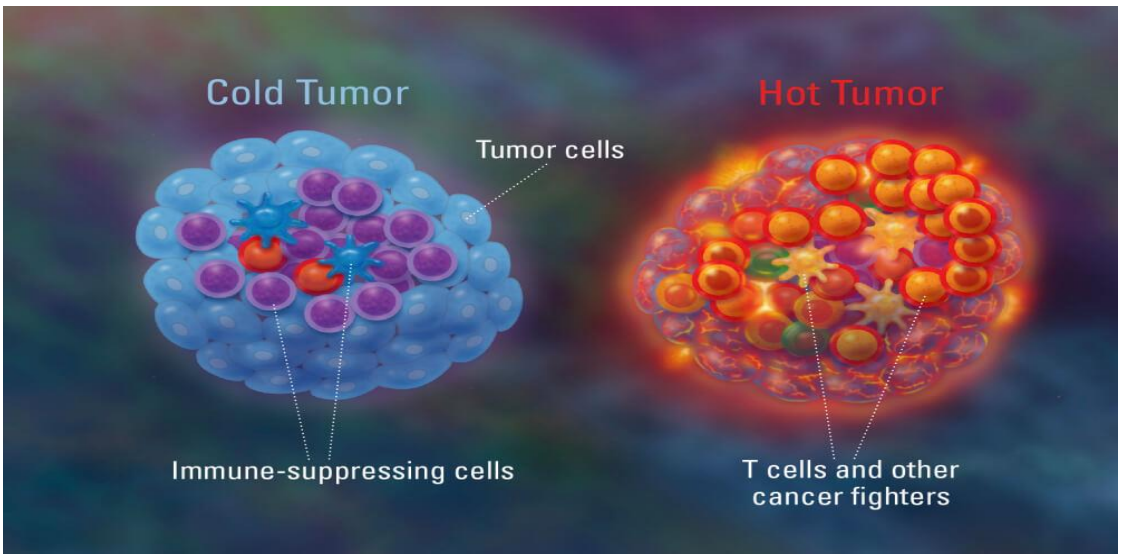



Image from the Dana-Farber Cancer Institute. https://blog.dana-farber.org/insight/2018/06/enhancing-immunotherapy-race-make-cold-tumors-hot/

As we begin 2022, I believe we are entering an exciting period of breakthrough clinical developments that will validate the LAG-3 opportunity the Immutep team has been sharing with investors for years. The turning point for this moment of clarity will be across the LAG-3 therapeutic space, as the FDA is expected to approve the first LAG-3 based therapy and numerous late-stage studies are slated to begin, including our program. Furthermore, the first ever LAG-3 summit in January was a great success.

Upcoming clinical milestones and corporate highlights:

- Ongoing recruitment and updates from TACTI-003
- Additional data from TACTI-002 (also designated KEYNOTE-798) is expected to be reported in the first half of calendar year 2022
- First interim results from INSIGHT-003 are expected to be reported in 2022
- Further regulatory interactions and manufacturing scale up to 2,000 L for efti
- Expansion of existing programs (including a planned Phase III trial for efti)
- Updates on IMP761

I look forward to updating you further on our progress in 2022, which we expect - and despite a great deal of volatility in the markets - will be a very exciting year for LAG-3 and Immutep!

# INDUSTRY CONFERENCES AND POSTER PRESENTATIONS

Scientific conferences have taken on a virtual format since the COVID-19 pandemic, and it has been good to be part of the industry's determination to push ahead with scientific innovation despite the challenges. The world needs new medicines now more than ever.

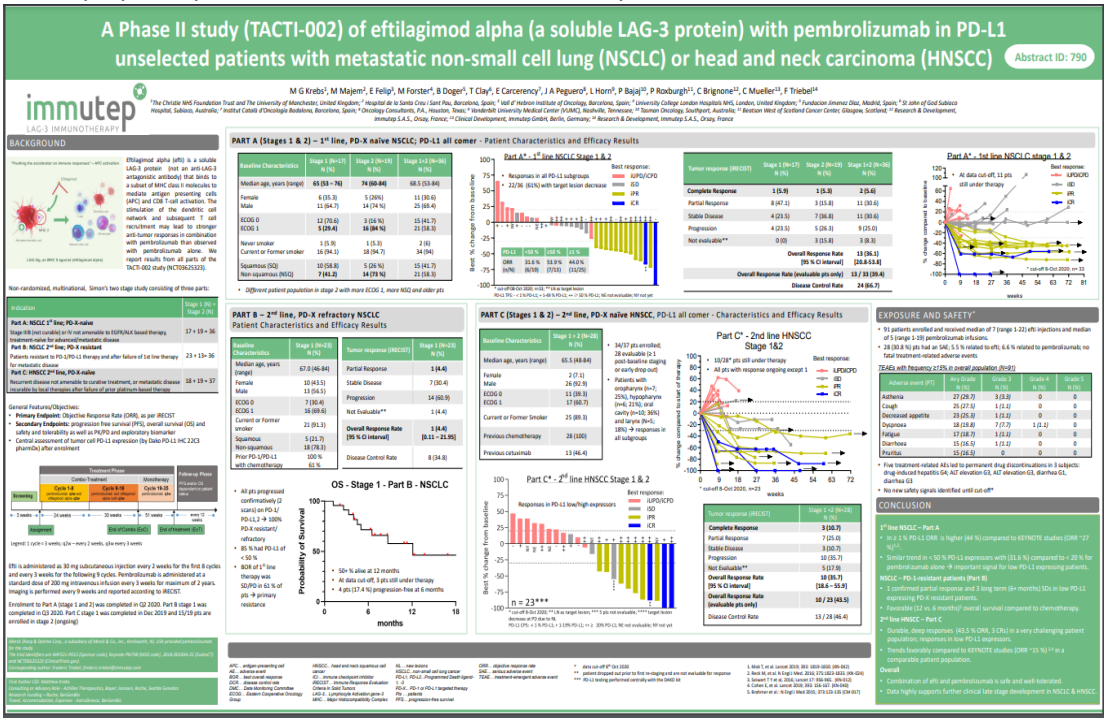
Immutep presented new and encouraging data from our ongoing Phase II TACTI-002 study at the Annual Meeting of the American Society of Clinical Oncology (ASCO) on 4-8th June 2021.

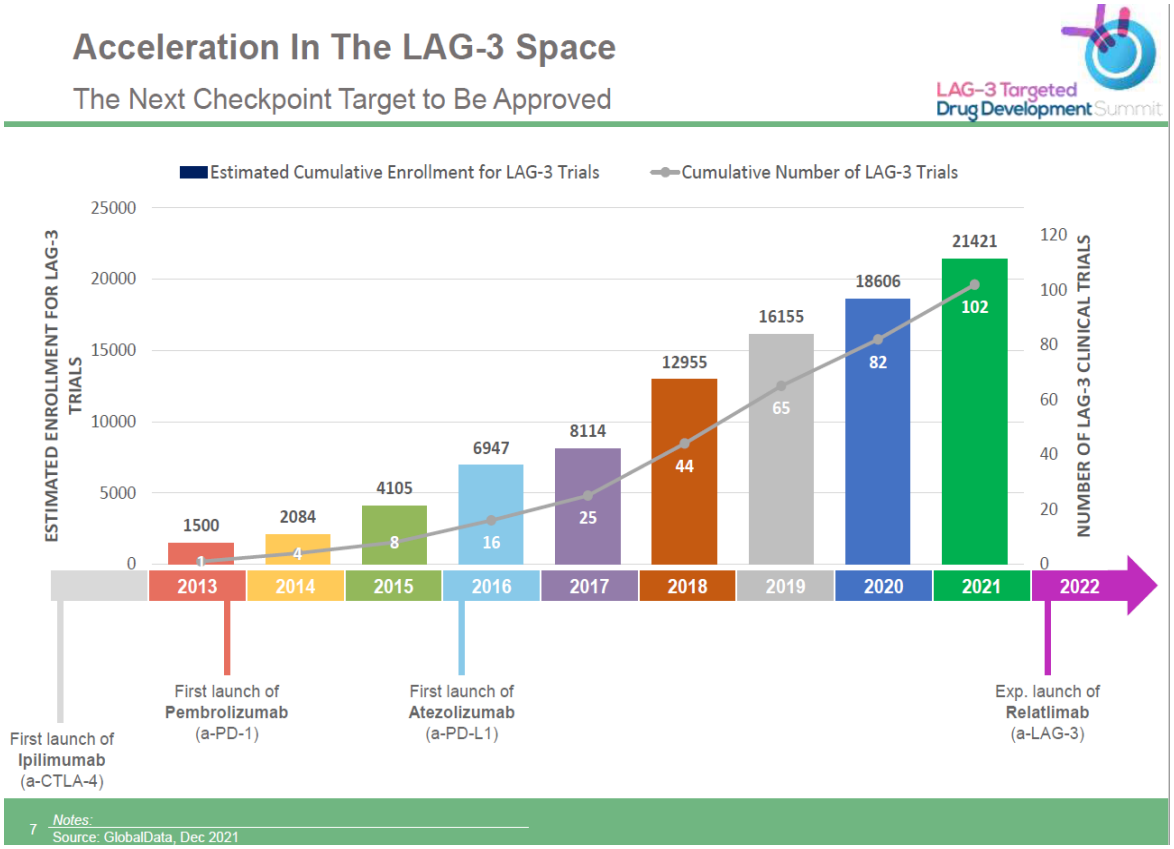
The data presented at ASCO is also summarised in the Operational Snapshot section of this newsletter.

Immutep was also pleased to present three posters at the Society for Immunotherapy of Cancer (SITC) Annual Meeting 2021 on 10-14th November 2021.

In particular, we presented final overall survival data from our Phase IIb AIPAC trial in a late breaker poster presentation. We also presented further interim data from TACTI-002 and the trial design of TACTI-003.

Please refer to https://www.immutep.com/investors-media/presentations.html for enlarged versions of Immutep's poster presentations and webcasts of the data presentations.






We were also delighted that CEO, Marc Voigt gave a company presentation and Frederic Triebel, Immutep Limited's CSO & CMO presented a keynote speech "My Journey Through the LAG-3/MHC Class II Landscape: 1988-2021" at the first ever LAG-3 Targeted Drug Development Summit in January 2022.

# OPERATIONAL SNAPSHOT

### AIPAC – Phase IIb study in breast cancer


Final results from AIPAC, a Phase IIb trial evaluating efti in combination with weekly paclitaxel in HR+ HER2- metastatic breast cancer, include statistically significant and clinically meaningful Overall Survival (OS) data in key patient subgroups, which support moving into Phase III clinical development.

Commenced planning for a new Phase III trial evaluating efti in metastatic breast cancer. Positive EMA scientific advice received in October 2021.

### TACTI-002 – Phase II study in solid cancers


Completed recruitment of patients (total of 185) across all cohorts of the Phase II study evaluating the combination of efti with MSD's KEYTRUDA® (pembrolizumab) in Australia, Europe and the US. The study is being conducted in collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada).

Interim data from Parts A and C of TACTI-002 in 1st line NSCLC and 2nd line HNSCC, respectively, were presented at ASCO in June 2021. The data were characterised by very favourable overall response rates (ORR) together with favourable duration and depth of responses. Multiple Complete Responses (complete disappearance of all lesions) were observed and tumor responses were seen in all PD-L1 subgroups, including low PD-L1 expressing patients which are typically less responsive to anti-PD-1 therapy.

Further interim data from Part C (2nd line HNSCC) were presented at SITC in November 2021. More data from TACTI-002 (including from Part A) will be reported in the first half of calendar year 2022.

### TACTI-003 – Phase IIb study in solid cancers


New randomised Phase IIb study evaluating efti in combination with MSD's KEYTRUDA® (pembrolizumab) in the commercially more relevant 1st line recurrent or metastatic HNSCC setting, including patients with PD-L1 negative and PD-L1 positive (CPS ≥1) tumors.

# OPERATIONAL SNAPSHOT

## INSIGHT – Phase I trial


INSIGHT is an investigator-initiated Phase I trial at the Institute of Clinical Cancer Research, Krankenhaus Nordwest (IKF) investigating different combination treatments with efti and a different route of administration for efti. The INSIGHT trial platform consists of 5 different arms from stratums A to E.

*INSIGHT-003 (Stratum C) – first triple combination therapy study with efti*
In August 2021, the first patient was enrolled in the Phase I INSIGHT-003 and by December 2021 the first five patients had been safely treated and evaluated for safety. Pleasingly, no additional safety signals were observed in the study which is the first time a triple combination therapy consisting of efti and an existing approved standard of care combination of chemotherapy (carboplatin) and an anti-PD-1 therapy has been administered. Patient recruitment is continuing with 6 out of a total of 20 patients with various solid tumours now participating in the trial. Interim results are expected to be reported in 2022.

*INSIGHT-004 (Stratum D) – efti in combination with avelumab in advanced solid cancer*
In June 2021, we reported final data for our INSIGHT-004 Phase I study at ASCO, which included promising activity signals from efti in combination with avelumab in a variety of difficult to treat solid cancers. Overall, 41.7% of patients responded to the therapy and half showed disease control. A good safety profile was also observed from treatment with the combination. This data was also presented at ESMO in September 2021. This trial was conducted under a collaboration and supply agreement with Merck KGaA, Darmstadt, Germany, and Pfizer.

*INSIGHT-005 (Stratum E) – efti in combination with bintrafusp alfa*
INSIGHT-005, known as stratum E of INSIGHT, will include 12 patients with solid tumours to evaluate efti in combination with bintrafusp alfa, an investigational bifunctional fusion protein immunotherapy. The study is a multi-centre, open-labelled Phase I/IIa trial in previously treated patients with different solid tumours and is under a collaboration and supply agreement with Merck KGaA, Darmstadt, Germany. However, in the light of the suboptimal results from Merck KGaA's bintrafusp alpha in other studies, this arm of the INSIGHT study is currently under review and might not go ahead.

## CYTLIMIC – Phase I in solid tumours

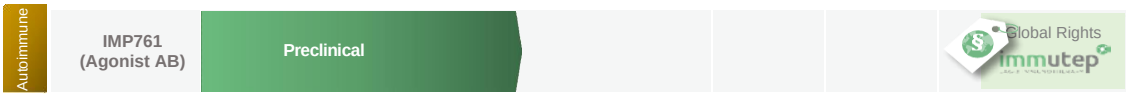

CYTLIMIC has been conducting Phase I studies with CYT001 which is CYTLIMIC's lead cancer vaccine. CYT001 comprises peptides designed using artificial intelligence from the HSP30 and GCP-3 proteins, plus two adjuvants, efti and Hiltonol (Poly-ICLC). Under the terms of clinical collaboration, service and supply agreements with Immutep, CYTLIMIC has full responsibility for the continued development of the cancer vaccine and Immutep is eligible to receive development-based milestone payments.

## EOC Pharma – EFTI


EOC Pharma has announced it plans to expand its clinical trial pipeline for efti (designated EOC202 in

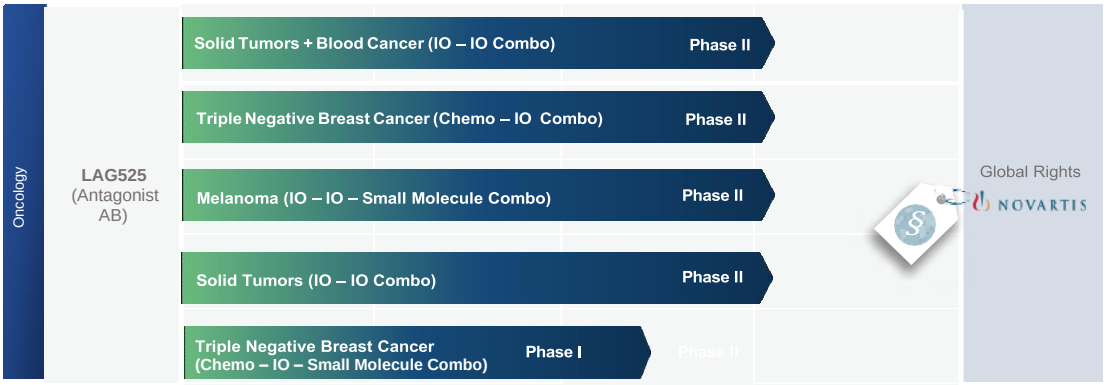
China) in China. EOC is preparing to initiate a clinical study of efti in combination with an anti-PD-1 therapy in the first half of calendar year 2022. This new trial builds on EOC's previously announced Phase II trial evaluating efti in combination with chemotherapy in metastatic breast cancer patients.

### IMP761 – Preclinical studies in autoimmune disease



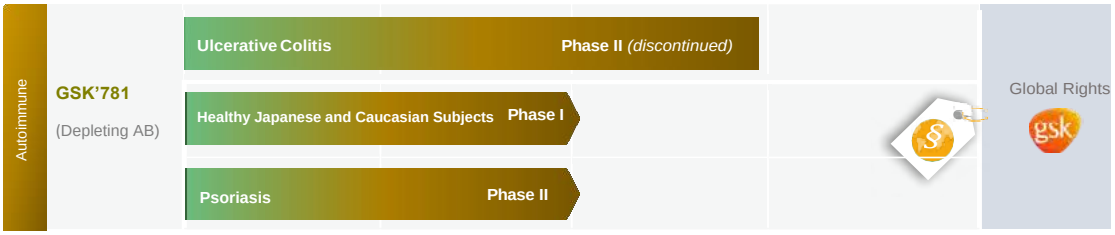

Our new preclinical product candidate IMP761 is being developed as the first known agonist antibody of LAG-3. It is a humanised IgG4 monoclonal antibody and is mechanistically distinct from any of the known LAG-3 antibodies. In December 2021, Immutep signed a Manufacturing Service Agreement with Northway Biotech to manufacture IMP761 ahead of clinical testing. Northway is developing a GMP-compliant manufacturing process of IMP761 in large scale bioreactors. The engineering and first GMP run at 200 L is planned to occur in early calendar year 2022 and should provide material for toxicology studies and a potential Phase I clinical trial in autoimmune diseases for IMP761.

### Novartis – LAG525




Novartis has five clinical trials for LAG525 in multiple cancer indications for more than 1,000 patients. Data was presented at the ESMO Congress in 2021.

### GSK – GSK'781




GSK conducted two successful Phase I studies. Their Phase II clinical study in up to 242 ulcerative colitis patients was discontinued, while further assessment is ongoing to determine next steps. Currently the partnership remains in place.

# OUTLOOK

Immutep continues to rapidly advance and expand the clinical development of our lead asset, efti, across multiple independent and collaborative clinical studies to treat various oncology indications, as well as scale up our manufacturing program. This expansion of our pipeline is being funded by the capital raise we completed in 2021 which attracted significant investor support and puts the company in a strong cash position. In addition, we have advanced our pre-clinical program in autoimmune disease over the last year.

Immutep‘s activity will step up again this year as we execute our development strategy for LAG-3 and transform into a late-stage biotech with more trials, partners and industry momentum. In doing so we will continue to align ourselves with many of the world’s largest pharmaceutical companies – including Merck, Pfizer, Merck MSD, Novartis, GSK, and EOC Pharma – through strategic development agreements. Not only does this validate our technologies, but it also demonstrates our strong track record of developing our assets.

We look forward to reporting our progress to you as Immutep steps onto the world stage as the leading LAG-3 pure-play biotech company. These updates will include reporting further clinical trial results from our Phase II TACTI-002 study of efti and first data from TACTI-003. In addition, we’ll be announcing regulatory progress and updates from our partnered programs.

COMPANY CALENDER

# What’s next

**FEBRUARY 14TH 2022 - FEBRUARY 17TH 2022**

**BIO CEO & Investor Conference**

Marc Voigt, CEO of Immutep will participate in the upcoming digital event.
https://www.bio.org/events/bio-ceo-investor-conference

**FEBRUARY 14TH 2022 - FEBRUARY 18TH 2022**

**11th Annual SVB Leerink Global Healthcare Conference**

Marc Voigt, CEO of Immutep, is scheduled to present a corporate overview.
https://www.svbleerink.com/events/

**MARCH 30TH 2022 - APRIL 2ND 2022**

**European Lung Cancer Congress 2022**

Immutep will participate in the online European Lung Cancer Congress 2022.
https://www.esmo.org/meetings/european-lung-cancer-congress-2022

**APRIL 4TH 2022 - APRIL 6TH 2022**

**BIO - Europe Spring**

Marc Voigt, CEO of Immutep will participate in the upcoming digital event.
https://informaconnect.com/bioeurope-spring/

**MAY 3RD 2022 - MAY 5TH 2022**

**ESMO Breast Cancer Congress 2022**

Immutep will attend the ESMO Breast Cancer Congress 2022.
https://www.esmo.org/meetings/esmo-breast-cancer-2022

**JUNE 3RD 2022 - JUNE 7TH 2022**

**ASCO 2022 Annual Meeting**

Immutep will attend the ASCO 2022 Annual Meeting.
*Venue: McCormick Place, Chicago, IL, USA*
https://am.asco.org/

IMMUTEP

# Fast Facts

**Listings**
Australian Securities Exchange (ASX), NASDAQ

**Stock Codes**
ASX: IMM, NASDAQ: IMMP

**Issued Capital – Ordinary Shares**
854.1 million (as of 16 Feb 2022)[1]

**Market Capitalisation**
~ A$324.57 million (US$232.97 million) (as of 16 Feb 2022)[2]

**Cash & Term Deposits**
~ A$99.66 million (US$72.31 million) (as of 31 Dec 2021)

## Board of Directors

**Russell J Howard, PhD**
Non-executive Chairman

**Marc Voigt**
Executive Director and Chief Executive Officer

**Pete A Meyers**
Non-executive Director and Deputy Chairman

## Senior Management

**Prof Frédéric Triebel, MD PhD**
Chief Medical Officer and Chief Scientific Officer

**Deanne Miller**
Chief Operating Officer, General Counsel and Company Secretary

**Christian Mueller**
Vice President Strategic Development

**Claudia Jacoby, PhD**
Director of Manufacturing

**James Flinn, PhD**
Intellectual Property and Innovation Director

**David Fang**
Finance Director & Assistant Company Secretary

(1) Currently ~27.81% of the ordinary shares are represented by ADSs listed on NASDAQ where 1 ADS represents 10 ordinary shares. Please refer to latest Appendix 2A released on ASX for a detailed summary of all securities on issue. (2) Market capitalisation based on ASX share price of A$0.38 on 16 February 2022. USD equivalent of cash balance was calculated with FX rate of 0.7256 and USD equivalent of market cap was calculated with FX rate of 0.7178.

**www.immutep.com**

# FOLLOW IMMUTEP'S PROGRESS

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

www.immutep.com

Our website is a treasure trove for those in search of details about our company, our management team, and archived information. We encourage everyone to check it out regularly.

**www.clinicaltrials.gov**

Immutep registers all of our clinical trials, and the details of enrolling doctors, on the ClinicalTrials.gov website, a service of the United States National Institutes of Health. This register is the largest such repository of clinical trial information around the world.

Our ClinicalTrials.gov ID for our trials are as follows:
- AIPAC trial is NCT02614833
- TACTI-002 trial is NCT03625323
- TACTI-003 trial is NCT04811027

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