IMUGENE
Developing Cancer Immunotherapies

ASX: IMU

Newsletter November 2021

CLINICAL TRIAL SUPPLY AGREEMENT WITH MERCK KGAA & PFIZER

02

CEO UPDATE

After yet another busy few months for Imugene in which we've taken several pivotal steps forward, I'm thrilled to bring you the latest edition of our shareholder newsletter.

Merck KGaA & Pfizer back HER-Vaxx combination study

A particularly exciting development just recently announced is the supply agreement we secured with Merck KGaA and Pfizer, that will see avelumab (BAVENCIO®) provided to Imugene for a Phase 2 clinical study of HER-Vaxx in HER2-positive gastric or gastroesophageal junction adenocarcinomas, also known as our neoHERIZON study.

To get support from major pharmaceutical players of this calibre is a particularly significant piece of validation for Imugene, and we are eager to see the results of HER-Vaxx alongside chemotherapy, with and without the FDA approved avelumab.

neoHERIZON is an open-label, multi-center, randomised, Phase 2 clinical trial designed to assess the safety and efficacy of perioperative (pre- and post-surgery) HER-Vaxx combined with chemotherapy with or without avelumab compared to chemotherapy alone in patients with HER2-positive gastric or gastroesophageal junction adenocarcinomas considered suitable for surgical resection.

As a primary endpoint we'll be hoping to see pathologic complete response, with secondary endpoints being safety and biomarker evaluation. Ultimately though, it is hoped that this forms another step in addressing the unmet needs of patients living with cancer. This and other updates on HER-Vaxx are detail below.

CHECKvacc enters the clinic as first patient dosed

In a major step forward for this program, we were very pleased to recently announce that our partner City of Hope had dosed the first patient in the Phase I clinical trial of our oncolytic virotherapy, CHECKvacc. The trial Is being conducted in patients with triple-negative breast cancer (TNBC), initially evaluating safety and evidence of efficacy of intratumoural administration of CHECKvacc against metastatic TNBC. The news came after our announcement in July that City of Hope had received Investigational New Drug (IND) approval from the FDA, allowing the commencement of the Phase I trial. After positive pre-clinical results we're eager to see how CHECKvacc performs in the clinic off the back of years of development led by Professor Yuman Fong and his team.
Dr. Yuan, MD PhD is the principal investigator on the study, a noted breast cancer specialist. In this issue of the newsletter we look further into CHECKvacc and the unmet need in TNBC.

Joining forces with Celularity & Eureka

Two new strategic developments we're incredibly excited by the potential of are the respective partnerships we've announced with Celularity and Eureka Therapeutics.

Celularity is a global pioneer in developing placental-derived allogeneic therapies available off-the-shelf. Combining our onCARlytics with Celularity's CyCART-19 will create a targeted approach to destroying solid tumours that could have applicability to a range of indications by enabling uniform expression of CD19. Along with the Celularity team, including world-renowned placental stem cell expert Dr. Robert Hariri, we are eager to push this strategic partnership to obtain a proof of concept of our CF33-CD19 (onCARlytics) in combination with CyCART-19 (CD19 directed CART).

Again harnessing the power of our onCARlytics technology, Eureka Therapeutics anti-CD19 ARTEMIS T-cell therapy will form another powerful combination to target treatment of solid tumours. By combining our technologies we have an excellent opportunity to address the lack of tumour-specific targets for T-cell therapies. We have already developed a real chemistry with the team at Eureka and look forward to taking our first steps on this collaboration, which we detail more below.

PD1-Vaxx Phase 1 continues

We've continued to see new patient recruitment in the Phase 1 clinical trial of our PD1-Vaxx immunotherapy, with important new steps over the coming months including ratification of the optimal biological dose (pending approval by the Cohort Review Committee). The initial signs have been encouraging, as we remain focused on safety and tolerability at this stage, early immune response signals have been seen. In this newsletter we dive deeper into the trial and checkpoint inhibitors.

A period of corporate milestones

As well as continuing to take important steps across our entire pipeline, we've secured our pathway forward with some key corporate developments in recent months, including a total of $95m capital raising and SPP and entry into the ASX300, which Paul will discuss in the 'From the Chair' section of the newsletter. Thanks to shareholders for their continued support, and we look forward to bringing you even more as we quickly approach 2022.

With warmest regards,

LESLIE CHONG
IMUGENE CEO

Combining our onCARlytics with Celularity's CyCART-19 will create a targeted approach to destroying solid tumours.

CELULARITY AND IMUGENE

Every once in a while, ground-breaking, cutting-edge technology winds up finding a pathway to the clinic and ultimately treating patients in a really exciting way, and this is one of those examples.

In August 2021, we joined forces with NASDAQ-listed Celularity to combine our CF33-CD19 oncolytic virus, known as onCARlytics, with Celularity's CD19 targeting allogenic CAR T cellular therapy, CyCART-19, to create a new and targeted approach to destroy solid tumours.

A spin-off of multibillion-dollar pharmaceutical giant Celgene, NASDAQ-listed Celularity develops off-the-shelf placental derived allogeneic cell therapies and is led by the revered Dr Robert Hariri, a pioneer in placental stem cell research.

With a focus across the cancer research community to enhance the immune system to recognise, attack, and destroy cancer cells.

Imugene's novel strategy to treat solid tumours uses onCARlytics to prime the tumour cells for destruction by eliciting the expression of validated tumour marker CD19.

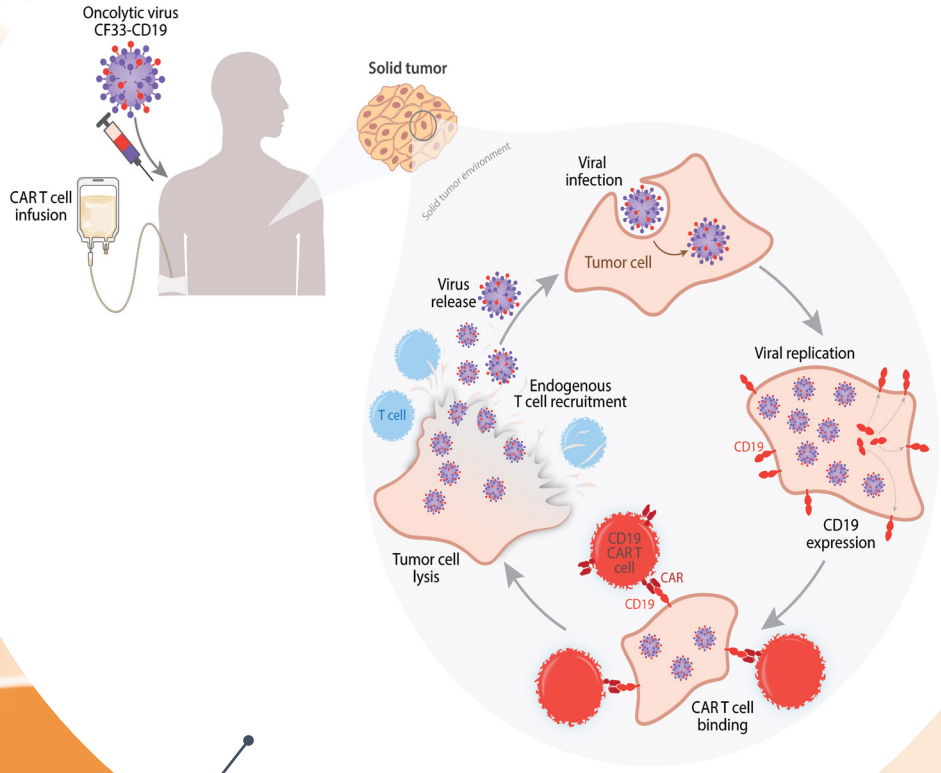
This new partnership will take that approach and then combine it with Celularity's CyCART-19 technology to destroy solid tumours.

CyCART-19 is a placental-derived T-cell investigational therapy engineered with a chimeric antigen receptor (CAR) that is cryopreserved, allogeneic and available off-the-shelf. CyCART-19 is in development initially for the treatment of B-cell malignancies, targeting the CD19 receptor.

Imugene had the pleasure of having Dr Hariri join us to discuss the collaboration, outlining why he saw outstanding potential for the drug combination.

We have already started collaborating on the non clinical in vitro and in vivo studies.

How does the CD19 Oncolytic Virus Work?



"The combination of the two is invaluable – it can literally set the stage for how to go after and treat a range of solid malignancies."

DR ROBERT HARIRI

EUREKA AND IMUGENE

With a range of high-quality biotechnology players around the world, and many working toward a common goal, we have continued discussions with numerous potential partners to drive Imugene's technologies forward. This can again be seen in our recently announced strategic collaboration with Silicon Valley based T-cell therapy business Eureka Therapeutics.

The collaboration again hinges on the unique ability of onCARlytics to cause solid tumours to express CD19, opening the door for a CD19 targeted therapy to combine with it and obliterate the tumour.

Eureka Therapeutics brings such a product to the table with its CD19 directed T-cell therapy ARTEMIS®, which has shown superior efficacy, enhanced tumour infiltration and less T-cell exhaustion in head-to-head pre-clinical studies against CAR-T cells. Building on the significant safety and efficacy data ARTEMIS has already delivered, there is potential to further enhance this using a combination approach.

Imugene and Eureka will kickstart the partnership with nonclinical in vitro and in vivo combination studies that will assist in driving a larger clinical development plan.

Asked what attracted Eureka Therapeutics to work with Imugene, Eureka's Founder and CEO Dr Cheng Liu said: "This onCARlytics mark and kill approach, to me it's brilliant, and it's a potential game changer for multiple reasons. It's a targetless approach, which means that once it works, you're not depending on the targeted profiling of the tumour, you can actually force the tumour to express the target you want and then you treat it with T-cell therapy to kill the tumour. So you can see the future market is no longer limited to any single tumour type."

Animal studies conducted at City of Hope showed the ability of onCARlytics to express CD19 in triple negative breast, pancreatic, prostate, ovarian, head and neck cancers, as well as brain tumours.

"This onCARlytics mark and kill approach, to me it's brilliant, and it's a potential game changer for multiple reasons."

DR CHENG LIU
EUREKA FOUNDER & CEO

CHECKVACC

About 15% of breast cancers are known as "triple negative", meaning they do not have any of the three validated and well-known receptors commonly found on breast cancer cells – due to this factor, treatment options are limited and TNBC is primarily treated with chemotherapy with high toxicity.

TNBC is also considered aggressive because it grows quickly, is more likely to have spread by the time it's diagnosed and unfortunately, more likely to return after treatment.

Imugene's oncolytic virotherapy CHECKvacc is aimed at providing an improved alternative, and recently announced dosing of the first patient in an investigator sponsored study of the drug in TNBC patients at City of Hope Comprehensive Cancer Center in Los Angeles. Per FDA requirements, dosing in the first cohort will require a minimum of 28 days between patient enrollment.

The trial is being led by Principal Investigator Dr. Yuan, MD PhD after IND approval was received from the US Food and Drug Administration (FDA) in July.

Oncolytic viruses (OVs) are designed to both selectively kill tumour cells and activate the immune system against cancer cells, with the potential to improve clinical response and survival. CHECKvacc is a chimeric vaccinia (pox) virus with hNIS and anti PD-L1 transgenes developed by Professor Yuman Fong, at the City of Hope.

The advantage of CHECKvacc is it directly delivers anti PD-L1 which allows the immune system to continue to recognise and kill cancer cells.

While oncolytic viruses offer promise in treating many cancers, CHECKvacc is targeting TNBC first, as Imugene believes there is huge unmet need in its treatment.

The trial aims to evaluate the safety and efficacy and determine the recommended Phase 2 dosage for intra-tumoural administration of CHECKvacc against metastatic TNBC.

Commencement of the clinical trial coincides with Breast Cancer Awareness Month, held each year in October.

"We are excited to be part of this important study and the search for effective new treatments for triple negative breast cancer, as there are limited options for patients"

DR YUAN.

Breast Cancer Statistics

20,000
Breast cancer is the most diagnosed cancer in Australia, with 20,000 people diagnosed over the past 12 months

15%
Triple negative breast cancer makes up about 15% of cases

3,000
About 3,000 Australians die as a result of breast cancer each year

1 in 7
1 in 7 Australian women are diagnosed with breast cancer in their lifetime

36%
Breast cancer diagnoses have increased 36% over the past 10 years

91%
Five-year survival rates continue to improve over the past 30 years and are now at 91% in Australia

Source: National Breast Cancer Foundation, https://nbcf.org.au/about-breast-cancer/breast-cancer-stats/

HER-VAXX

As the first cancer therapy that entered the clinic for Imugene, we are excited to announce important progress achieved on our HER-Vaxx program in the past few months.

HER-Vaxx is a B-cell peptide cancer immunotherapy designed to treat tumours that overexpress the HER-2/neu receptor, such as gastric, breast, ovarian, lung and pancreatic cancers. In pre-clinical and Phase 1 and 2 studies, HER-Vaxx has demonstrated potential to stimulate a potent polyclonal antibody response to HER-2/neu, a well-known and validated cancer target, which promotes the immune system to fight the growth of cancer cells.

Recently we announced a clinical trial supply agreement with Merck KGaA and Pfizer, which will evaluate the safety and efficacy of HER-Vaxx in combination with BAVENCIO® (avelumab) in patients with HER2-positive gastric cancer.

The study, to be known as neoHERIZON, is an open-label, multi-center, randomised, Phase 2 clinical trial designed to assess the safety and efficacy of perioperative (pre- and post-surgery) HER-Vaxx combined with chemotherapy with or without avelumab compared to chemotherapy alone in patients with HER2-positive gastric or gastroesophageal junction adenocarcinomas considered suitable for surgical resection.

HER-Vaxx has already shown a favorable safety profile and encouraging efficacy in patients with gastric cancer. Now working with Merck KGaA and Pfizer to evaluate the combination of HER-Vaxx with avelumab, an immune checkpoint inhibitor, will allow us to understand the potential synergy in this unmet need for people living with cancer.

This research partnership followed news that we'd been granted a patent for HER-Vaxx in Japan. This is an important milestone which adds extra value to our portfolio of B-cell immunotherapies as well as providing protection for our work in a major HER2-positive gastric cancer market – Japan has the third highest incidence rate of gastric cancers worldwide.

We have also announced news that HER-Vaxx achieved secondary efficacy endpoint progression free survival (PFS) data in HER2-positive gastric cancer, after a Phase 2 clinical trial which saw 24 of the 36 enrolled patients achieve a PFS event.

There are plans for further Phase 2 studies focusing on gastric cancer, which includes the neoHERIZON study as well as the nextHERIZON and neuHERIZON studies.

BAVENCIO® avelumab Injection 20 mg/mL

- **Developed and commercialised under a strategic alliance between Merck and Pfizer formed in 2014**
- **FDA approved for treatment of merkel cell carcinoma, renal cell carcinoma and urothelial cancer**
- **A man-made antibody that strengthens the immune system to fight cancer**
- **Now approved in 50+ countries with sales estimated to reach US$800m**

Image of drug source: https://www.merckgroup.com/en/expertise/oncology/oncology-treatments/bavencio

PD1-VAXX

Checkpoint inhibitors are offering new hope in the treatment of aggressive cancers, and research into their use continues to gain momentum, with more than 1,500 clinical trials underway around the world to determine their effectiveness.

Checkpoint inhibitors work by prompting a patient's immune system so that immune cells recognise and attack tumours. There are several treatments already in the market, such as Keytruda® and Opdivo®, that deliver monoclonal antibodies which can fight cancer.

Imugene is researching B-cell activating immunotherapy technology, including PD1-Vaxx which is designed to treat tumours by interfering with the interaction between PD-1, or "programmed death 1", a T-cell receptor and PD-L1, a protein that stops the immune system's response to cancer.

Imugene is testing an immunotherapy called PD1-Vaxx, with the first in-human, Phase 1 multi-centre dose escalation study underway across six sites worldwide, involving patients with non-small cell lung cancer who have progressed on previous treatment.

Developed by Professor Pravin Kaumaya at the Ohio State University in Columbus OH, PD1-Vaxx is constructed from a single B cell epitope derived from the extracellular domain of PD-1. PD1-Vaxx is designed to allow the immune system to win the battle against cancer by turning the body into an antibody producing factory. This prompts the body's T-cells to mount an attack on the cancer.

The primary goal of the Phase 1 trial is to determine safety and an optimal biological dose (OBD), as well as measuring efficacy, tolerability and immune response. Determination of OBD will be made by the Cohort Review Committee, and requires successive dosing within cohorts of at least three patients each.

PD1-Vaxx is showing early signs of an immune response in patients, according to study results to date, with antibodies to the target biomarker PD-1 evident in validated assays. Clinicians have reported no safety, toxicity or tolerability issues with PD1-Vaxx so far during the study.

With three patients having commenced their dosing schedule for the third monotherapy cohort of the Phase 1 trial, Imugene is moving closer to a major milestone in its PD-1 research.

In its next steps, Imugene will progress the study into combination escalation and expansion with up to 30 patients.

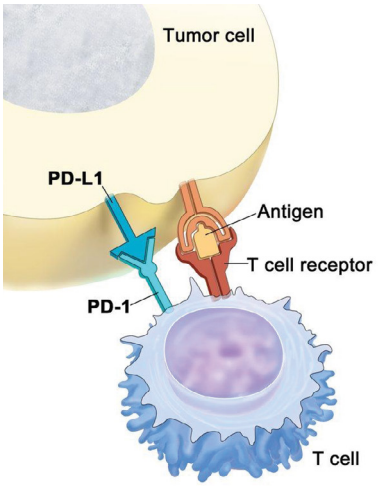
Estimated PD-1/PDL-1 Market Size and Evaluation

Drug	Name	Company	Status	Sales Estimate 2024 (USD $B)
Pembrolizumab	Keytruda®	Merck	Approved	**$22.32**
Nivolumab	Opdivo®	Bristol Myers	Approved	**$10.52**
Atezolizumab	Tecentriq®	Roche	Approved	**$5.29**
Avelumab	Bavencio®	Pfizer	Approved	**$1.7**
Durvalumab	Imfinzi®	AstraZeneca	Approved	**$4.22**
Total For Market*				**$47.33B**

Source: https://www.rncos.com/Market-Analysis-Reports/Global-Immune-Checkpoint-Inhibitors-Market-Outlook-2022-IM926.htm

The global immune checkpoint inhibitors market is expected to cross US$25 billion next year, according to a 2018 report by RNCOS. In addition, checkpoint inhibitors are likely to account for a major percentage of total cancer immunotherapy revenue within 10 years.

PD-L1 binds to PD-1 and inhibits T cell killing of tumour cell



Blocking PD-L1 or PD-1 allows T cell killing of tumour cell

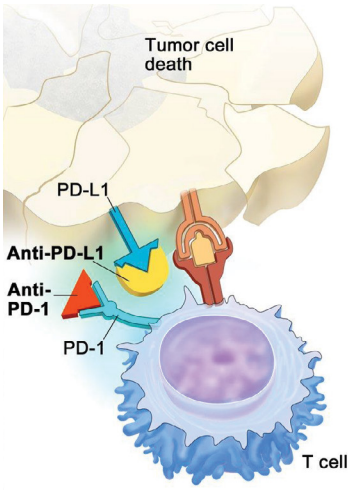


Figure 1 - PD1-Vaxx is an anti-PD-1 targeting immunotherapy which interferes with the interaction between the PD-1 T-cell receptor and PD-L1, a protein that stops the immune system's response to the tumour cell Source: https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors

FINANCE

Financial Snapshot
(as at 12 November 2021)

ASX code	IMU
Market cap	$3.17B
52 week high/low	61.25c/7.6c
Cash balance	$112.2M 30 Sept 2021
Industry	Biotechnology

Note: All figures are in Australian dollars. Market capitalisation calculations based on ordinary shares (5.6631b) only and excludes the dilutive impact of options outstanding (568m).

Top 5 shareholders
(as at 14 September 2021)

Citicorp Nominees	5.96%
Richard Mann and Assoc.	5.35%
Paul Hopper	5.34%
HSBC Custody Nominees	3.35%
Dr Nicholas Smith	2.16%

Board & Management

Directors

Mrs Leslie Chong
Chief Executive Officer & Managing Director

Mr Paul Hopper
Executive Chairman

Mr Charles Walker
Non-Executive Director

Dr Lesley Russell
Non-Executive Director

Dr Jens Eckstein
Non-Executive Director

Senior Management

Dr Nick Ede
Chief Technology Officer

Dr Monil Shah
Chief Business Officer

Dr Rita Laeufle
Chief Medical Officer

Dr. Anthony Good
Vice President of Clinical Research

Mrs Amanda Seiz
Senior Director Clinical Operation Head

Ms Bonnie Nixon
Project Manager

Mr. Phillip Hains
Company Secretary

Scientific Advisory Board

Dr Josep Tabernero
President ESMO, Vall d'Hebron University Hospital Spain

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OSU, USA

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Medical University of Vienna

Dr Tanios Bakaii-Saab
Mayo Clinic USA

Dr Neil Segal
MSKCC USA

Dr Yelena Janjigian
MSKCC, USA

Prof Peter Schmid
Barts Cancer Institute at Queen Mary University London

OV Scientific Advisory Board

Dr Yuman Fong
City of Hope, USA

Dr Saul Priceman
City of Hope, USA

Prof Prasad Adusumilli
MSKCC, USA

Dr Rebecca Auer
Ottawa Hospital, Canada

FROM THE CHAIR

I'm proud to be writing this latest update following what has been a truly transformational period for Imugene. While there has been some pleasing successes in recent times, the team and I remain strongly focused on the ultimate goal of developing revolutionary immunotherapies and delivering shareholder value along the way.

An integral and often challenging part of building a biotechnology company is raising the typically large amounts of capital required to fund clinical development. This makes our recent placement and share purchase plan, raising a total of $95m, such an outstanding achievement for Imugene.

The funds from this round provides the company with the cash runway to cover Imugene's entire clinical trial pipeline through to the end of 2025, not accounting for other potential revenue streams that may arise. It also brought a new class of institutional investor onto the Imugene register, and we thank these new shareholders as well as existing shareholders who supported the capital raising for their support.

The progress and growth of Imugene over the last 12 months led to our recent addition to the S&P/ASX 300 Index, an important achievement that is not only reward for the significant effort of our team, but also sees our company more widely held by index funds and having an increased profile amongst the business and investment community.

We have also made important moves from a personnel perspective, including the recruitment of US-based Chief Business Officer Dr Monil Shah. His experience and connections are already proving to be invaluable to the company.

With numerous irons in the fire that hold incredible potential at Imugene, we will continue to bring you news via the ASX and our electronic channels, and encourage you to stay across all the latest developments as they come to hand.

With kind regards,

PAUL HOPPER

IMUGENE
Developing Cancer Immunotherapies

ASX: IMU

About

Imugene is a clinical stage immuno-oncology company developing a range of new treatments that seek to activate the immune system of cancer patients to identify and eradicate tumours.

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