IMUGENE

Developing Cancer Immunotherapies

ASX:IMU

POSITIVE OS DATA IN HER-VAXX PHASE 2 TRIAL

July 2022

WE HAVE CONTINUED TO PROGRESS OUR OUTSTANDING CLINICAL PIPELINE.

Leslie Chong
Imugene CEO & Managing Director

CEO UPDATE

I'm delighted to bring you the latest edition of our shareholder newsletter after another productive period for Imugene, over which we have achieved numerous important milestones. We have continued to progress our outstanding clinical pipeline while building an experienced and credible management team whose skills will be imperative to our next phase of growth. This includes the recent appointment of our Executive Director, Clinical Scientist Dr Sharon Yavrom, who we'll profile in our next newsletter.

HER-Vaxx OS results highlight safety and efficacy

Recently we were pleased to report positive final overall survival data from our Phase 2 study of HER-Vaxx in advanced gastric cancer patients. The results added to our confidence in the potential for the B-cell immunotherapy, continuing to demonstrate safety and efficacy when compared to standard of care chemotherapy. This is an important milestone for the HER-Vaxx program, and we now look forward to the findings from our nextHERIZON and neoHERIZON combination trials commencing soon.

VAXINIA (CF33) Phase 1 trial commencing

Imugene is excited to be embarking on a Phase 1 clinical trial of VAXINIA in metastatic advanced solid tumours after receiving the relevant regulatory approvals in March. The first clinical site, the renowned City of Hope® Cancer Research Center, dosed the first patient in the trial during May. We are thrilled to be partnering with an institution of the caliber of City of Hope® on another clinical trial and look forward to working with its eminent team of experts. The trial will be rolled out to other sites across the USA and Australia throughout 2022.

PD1-Vaxx trial completes monotherapy dose escalation

Since the last update, we have also made excellent progress on several therapies in our clinical pipeline. The first of these is the clinical trial of our B-cell activating immunotherapy, PD1-Vaxx, which has been deemed safe after it was administered as monotherapy in patients at three different doses. This allows the trial to progress to the next stage, Phase 1b, where PD1-Vaxx will be administered in combination with Atezolizumab (TECENTRIQ®) in lung cancer patients. Atezolizumab will be provided by Roche for this stage of the study. This is an area of great interest within the industry and we look forward to sharing the results with you in future updates.

CHECKvacc trial progresses to second patient cohort

The first-in-human Phase 1 study of breast cancer oncolytic virotherapy CHECKvacc has also passed an important milestone. Because no previous studies have been carried out in patients, our clinical trial partner City of Hope®, a pre-eminent cancer research and treatment organisation in the United States is using a particularly conservative approach where a single patient is administered CHECKvacc, with a 28-day window to observe for adverse reactions before it is administered to a second patient. We are pleased to report that the first three patients, who form the first cohort, have not had any serious adverse reactions and no dose-limiting toxicities have been observed, which means the trial will now move to the second cohort of patients.

Ethics approval paves way for Phase 2 HER-Vaxx trial

Recently we were pleased to receive the required approval that allows us to commence our nextHERIZON Phase 2 clinical trial of HER-Vaxx in Australia. Targeted at HER2-positive metastatic gastric cancer patients and commencing at the Queen Elizabeth Hospital in Adelaide, the study will investigate the safety and response rate of HER-Vaxx in combination therapy and will also consider duration of response, progression free survival, overall survival, and biomarker evaluation.

Management team strengthened by new additions

The Board have made the strategic decision to bolster our management team in recent months, with a view to securing the right skills and experience to support the next phase of Imugene's growth.

To this end, please join us in welcoming Ursula McCurry as Senior Vice President of Clinical Operations and Dr Nimali Withana as Senior Director of Clinical Science. Both have impressive credentials in their respective fields and extensive industry experience over many years. We are proud to have them join Imugene and hope that you will take the opportunity to learn more about them in this newsletter.

Continued corporate achievements

In addition to furthering our clinical pipeline and bolstering our management team, we have continued to make headway in the corporate space. Two key achievements include our entry into the ASX200 in December and the receipt of a substantial R&D tax incentive from the Australian Government for our work last financial year. Paul discusses both these achievements in his 'From the Chair' section of the newsletter.

Thank you to all of our shareholders for the confidence and trust you have placed in us. We aim to continue providing you with ongoing value and look forward to keeping you updated on Imugene's progress in 2022.

POSITIVE OS DATA IN HER-VAXX PHASE 2 TRIAL

Register

Watch Dr Tanuj Chawla and consulting statistician Brent Blumenstein discuss the outcomes

https://bit.ly/3afxqsD

KEY RESULTS

41.5%

Survival benefit for patients treated with HER-Vaxx plus standard of care (SOC) chemotherapy compared to SOC chemotherapy alone.

13.9 months

Median overall survival for patients receiving HER-Vaxx plus chemotherapy, compared to 8.3 months in patients treated with chemotherapy alone.

0.585

Overall survival HR (80% 2-sided CI: 0.368, 0.930) with a statistically significant p-value of 0.066.

No toxicity

No difference in safety events between the two treatment arms, suggesting that HER-Vaxx does not add toxicity to SOC chemotherapy.

Completion of a Phase 2 trial is a major achievement for any biotechnology company, and Imugene was pleased to announce the final analysis results of its HERIZON clinical study that investigated Imugene's HER-Vaxx B-cell immunotherapy in advanced gastric cancer (Her-2/Neu overexpressing advanced/metastatic gastric/GEJ cancer).

The positive impact led to the survival of some patients by up to almost three years after starting therapy. The HERIZON study was designed to measure the efficacy, safety and immune response in patients with metastatic gastric cancer overexpressing the HER-2 protein. The study was randomised into two arms of either HER-Vaxx plus SOC chemotherapy or SOC chemotherapy alone. The primary endpoint was overall survival and secondary endpoint was progression-free survival. Safety, tolerability and immune response was also measured.

The Phase 2 trial was conducted at multiple sites across Eastern Europe and India where clinicians have difficulty accessing approved antibody treatments such as Herceptin® and Perjeta®, marketed by Swiss multinational Roche.

In conjunction with the announcement of the OS data, Imugene also advised that the HERIZON-extension Cohort Review Committee (CRC) has confirmed a new higher dose of HER-Vaxx (100µg) has been approved for use in the nextHERIZON and neoHERIZON studies commencing soon.

The CRC unanimously agreed the higher dose to be safe with no dose-limiting toxicities and no serious adverse reactions observed, and this is expected to accelerate and strengthen antibody generation to further improve the clinical response for HER-Vaxx. Drug supply was also confirmed with completion and delivery of a large-scale batch of HER-Vaxx from manufacturer piCHEM in Austria.

Upon announcing the results, we were pleased to welcome Principal Investigator Dr Tanuj Chawla and consulting statistician Brent Blumenstein to discuss the outcomes with shareholders, investors and interested parties.

FIRST PATIENT IN FOR VAXINIA PHASE 1 TRIAL

VAXINIA is Imugene's lead oncolytic virotherapy for the treatment of solid tumours, which was developed by the lab of Professor Yuman Fong, the Sangiacomo Family Chair in Surgical Oncology at City of Hope®, and a noted expert in the oncolytic virus field.

Oncolytic viruses are designed to both selectively kill tumour cells and activate the immune system against cancer cells, with the potential to improve clinical response and patient outcomes.

Aimed at improving the outcomes of patients with advanced solid tumours, preclinical laboratory and animal models to date have shown the ability of VAXINIA to shrink colon, lung, breast, ovarian and pancreatic cancer tumours.

In March, we achieved a new milestone for VAXINIA when we received approval from the Western Institutional Review Board (WIRB) to commence a world first Phase 1 clinical trial in multiple solid tumours in patients. The US component of the Phase 1 trial will be conducted under the Food and Drug Administration (FDA) investigational new drug (IND) process, which gave approval for the trial in December 2021.

IN MAY, CITY OF HOPE® DOSED THE FIRST PATIENT IN THE PHASE 1 TRIAL.

The study aims to recruit 100 patients across 10 trial sites in the United States and Australia with City of Hope® being the first study site.

The trial will run for 24 months and be led by Principal Investigator, Dr Daneng Li MD, an assistant professor in the Department of Medical Oncology and Therapeutics Research at City of Hope®, and a respected expert in gastrointestinal cancer.

The multi-centre phase 1 trial will deliver a low dose of VAXINIA to patients who have been treated with at least two prior lines of standard of care treatment, with an injection directly into the tumours or intravenously. Once acceptable safety is demonstrated at the lowest doses, certain new study participants will receive VAXINIA in combination with approved immunotherapy Pembrolizumab.

The clinical trial is titled "A Phase I, Dose Escalation Safety and Tolerability Study of VAXINIA (CF33- hNIS), Administered Intratumourally or Intravenously as a Monotherapy or in Combination with Pembrolizumab in Adult Patients with Metastatic or Advanced Solid Tumours (MAST)."

New clinical trial sites added to the study, in addition to further information, can be found at: clinicaltrials.gov/ct2/show/NCT05346484

FDA INVESTIGATIONAL NEW DRUG APPROVALS

In December, Imugene achieved US Food and Drug Administration (FDA) Investigational New Drug (IND) approvals for two different immuno-oncology therapies in our portfolio.

The FDA IND gave us approval to initiate a new phase 2 clinical trial of HER-Vaxx to study safety and efficacy of this immunotherapy candidate in combination with chemotherapy or Pembrolizumab (KEYTRUDA®) in patients with advanced gastric cancer.

Simultaneously, we also received the FDA IND approval to initiate a Phase I clinical trial of our oncolytic virotherapy candidate, VAXINIA (CF33-hNIS, HOV2). This allowed Imugene to start patient recruitment and dosing in a Phase 1 clinical trial for the Metastatic or Advanced Solid Tumours study in multiple solid tumour type patients.

PD1-VAXX PHASE 1 TRIAL PROGRESSES TO COMBINATION DOSE ESCALATION

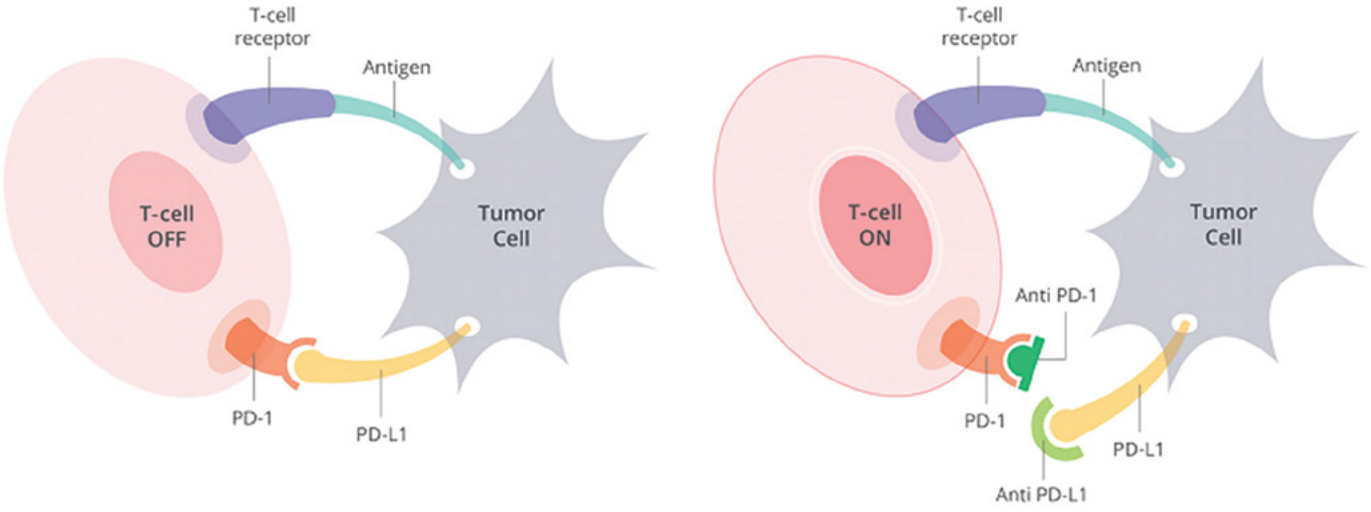
Imugene is conducting a clinical trial on PD1-Vaxx, a B-cell activating immunotherapy technology which is designed to treat tumours by interfering with the interaction between PD-1, or "programmed death 1", a T-cell receptor and PD-L1, a protein that stops the immune system's response to cancer. Phase 1 of the trial is being performed in several stages and is designed to look for safety, tolerability and early response signals to determine the optimal dose for further development.

In January we were pleased to announce that the Cohort Review Committee (CRC) confirmed PD1-Vaxx had completed the monotherapy dose escalation of the clinical trial. The Phase 1a monotherapy dose escalation was performed with 10, 50 and 100µg of PD1-Vaxx in non-small cell lung cancer (NSCLC) patients who progressed on one or more immune checkpoint inhibitors (ICIs).

After the CRC reviewed the safety, tolerability and biomarker data of the monotherapy, it advised Imugene to proceed to the combination phase of clinical development of PD1-Vaxx.

The targeting of PD-1/PD-L1 proteins with combination therapies is an area of promise within the pharmaceutical industry. Dual therapies that use PD1-Vaxx in combination with monoclonal antibody therapies such as Atezolizumab (TECENTRIQ®), may have the potential to extend the treatment of the monoclonal antibodies. This type of combination therapy has an advantage over the combination of two monoclonal antibodies because it induces a unique polyclonal immune response which may increase response rates for the combination therapy.

We're encouraged that we are seeing positive signals at such an early stage of our PD1-Vaxx Phase 1 trial and are excited about progressing to the Phase 1b combination studies in treatment naïve patients.



CHECKVACC PHASE 1 TRIAL PROGRESSES TO SECOND COHORT

CHECKvacc is an oncolytic virotherapy that is aimed at providing an improved alternative to patients suffering from "triple negative" breast cancer (TNBC). These patients, who comprise about 15% of all breast cancer patients, suffer from an aggressive form of breast cancer that also does not exhibit any of the three well-known receptors commonly found on breast cancer cells. As a result, treatment options are currently limited and TNBC is primarily treated with chemotherapy of high toxicity.

In late 2021, we partnered with City of Hope® to carry out the first-in-human, Phase 1, single-centre, dose escalation study of CHECKvacc. The FDA specified a 28-day stagger between patient dosing so the trial design will involve a dose escalation in individual patients, followed by an expansion to 12 patients at the final dose, which will be the recommended phase 2 dose.

In December, we were pleased to announce that the first patient had cleared the 28-day safety window between patient dosing, allowing City of Hope® to administer CHECKvacc on a second patient. The trial has continued to make excellent progress in early 2022 after the Cohort Review Committee reviewed all safety and tolerability data for the first three patients, who were given the with lowest dose of CHECKvacc as monotherapy. The Cohort Review Committee determined CHECKvacc to be safe with no dose-limiting toxicities and no serious adverse reactions observed.

City of Hope® has now proceeded with opening the second CHECKvacc Phase 1 cohort. We look forward to continuing this study and reporting our progress to our stakeholders.

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NEW MANAGEMENT PROFILES

URSULA McCURRY

Ms McCurry commenced her role as our Senior Vice President of Clinical Operations on 1 January 2022 after a long career as a clinical operations leader with over 20 years' global clinical development experience across a number of established and emerging biotech and pharmaceutical companies including Genentech, Exelixis, Astex, QLT Inc and Amunix.

Prior to joining Imugene, Ursula served as the VP of Clinical Operations at Amunix Pharmaceuticals and prior to that she was a Clinical Program Director at Genentech, leading multiple programs from entry into the clinic to phase three development, including taselisib and GDC-9545. She has also led the Drug Safety teams, ensuring quality, compliance, pharmacovigilance, and safety reporting.

Ursula received a Master of Arts degree from Simon Fraser University and a certificate in Biotechnology, Clinical Trial Design and Management from San Francisco State University.

DR NIMALI WITHANA

Dr Nimali Withana commenced her role as Imugene's Senior Director of Clinical Science on 1 January 2022. Dr Withana has over 18 years of drug development experience spanning both academia and industry.

Most recently she was the Lead Country Medical Manager for the Breast Cancer and Cancer Immunotherapy portfolios including bevacizumab, trastuzumab emtansine, ipatasertib and Atezolizumab at Hoffman-La Roche New Zealand. Prior to this, she was the Clinical Scientist Lead across Phase I – III global oncology trials at Genentech. Her experience has given her an in-depth understanding and grasp of the development process with experience in R&D, Clinical Trials and Patient Advocacy.

Dr Withana received her academic training at Stanford University and The Peter MacCallum Cancer Centre, majoring in Immunology and Molecular Medicine.

DR YANGHEE WOO

Imugene was pleased to add renowned surgeon-scientist Dr Yanghee Woo to its Scientific Advisory Board in June.

Dr Woo is Surgical Oncologist and Associate Professor of Surgery at City of Hope®, also holding key roles as Director of GI Minimally Invasive Therapies Program and Vice Chair of International Affairs.

Her clinical expertise in robotic surgery and gastric cancer is backed by research in gastric cancer inception and viral oncolytic therapy based on the CF33-platform.

Dr Woo was previously at Columbia University Medical Center's (CUMC) Pancreas Center where she was Assistant Professor of Surgery and later Director of Center for Global Excellence in Gastric Cancer Care.

Dr Woo completed her Medical Doctorate at Drexel University Medical School, completed the Health Careers Program at Harvard University, a general surgery residency at CUMC, a research fellowship at Memorial Sloan Kettering Cancer Center and a clinical fellowship at Severance Hospital, Yonsei University in Seoul, South Korea.

PHASE 2 OF NEXTHERIZON STUDY OF HER-VAXX RECEIVES ETHICS APPROVAL

In May, the Human Research Ethics Committee (HREC) approved for Imugene to commence a Phase 2 clinical trial of HER-Vaxx in Australia on patients with metastatic HER2-positive gastric cancer.

In order to obtain ethics approval, we demonstrated that we had successfully completed all necessary preclinical safety and efficacy testing of HER-Vaxx required to commence an open-label, multi-centre, signal generating, Phase 2 clinical trial designed to assess the safety and efficacy of HER-Vaxx in combination with chemotherapy or Pembrolizumab. The study aims to evaluate the safety and response rate of HER-Vaxx in combination therapy and will also consider duration of response, progression free survival, overall survival, and biomarker evaluation.

The first site of the phase 2 trial is the Queen Elizabeth Hospital in Adelaide under the direction of Principal Investigator Dr Tim Price. We anticipate additional clinical sites will be opened in Australia, and also in the US under Food and Drug Administration (FDA) investigational new drug (IND) approval.

PD1-VAXX & CHECKVACC SCIENCE SERIES

Imugene kickstarted a new initiative in late 2021 with our Science Series webinars, providing shareholders and interested parties with the opportunity to take a deeper dive on the people and science behind Imugene's clinical pipeline.

Imugene's CEO Leslie Chong, Senior Director of Clinical Science Dr Nimali Withana and Professor Pravin Kaumaya from the Ohio State University then discussed **B cell immunotherapy PD1-Vaxx at the second installment of our Science Series.**

Follow the link to watch the full Webinar:
https://youtu.be/tSkREkYJVgs

Our CEO Leslie Chong, Professor Yuman Fong and Dr. Yuan Yuan from City of Hope® Cancer Research and Treatment Center got the first Science Series event underway when they discussed **Imugene's oncolytic viral therapy CHECKvacc.**

Follow the link to watch the full Webinar:
https://youtu.be/UtMVyITUU9E

SOLIDIFYING IMUGENE'S INTELLECTUAL PROPERTY POSITION

In recent months, we're pleased to have further strengthened our intellectual property protection of the immuno-oncology therapies in our clinical pipeline, across key international markets. In January, we received a Notice of Grant from the Japanese Patent Office which protects the CF33 family of oncolytic viruses, including VAXINIA (CF33-hNIS) and CHECKvacc (CF33-hNIS-antiPDL1), through to 2037.

We were also granted patents from the relevant patent offices in Europe, China and South Korea to protect our HER-Vaxx immunotherapy to 2036. This is an important achievement as approximately 75% of all gastric cancer diagnoses are in Asia with particularly high rates of occurrence in East Asia, making China a very large market for gastric cancer medications. In addition, Europe is also another major pharmaceutical market.

FROM THE CHAIR

Paul Hopper
Executive Chairman

I'm pleased to be providing you with an update after another busy period for Imugene during which the team has continued to work steadfastly towards achieving our mission of developing transformative cancer medicines to improve patients' lives and to establish value and trust with our stakeholders.

We have rapidly progressed as an immuno-oncology company in recent months and a great testament of this growth is Imugene entering the S&P/ASX 200 index in late 2021 after entering the S&P/ASX 300 Index only a short time before that. This is a reflection of the way we have been able to advance our clinical pipeline, commercial achievements and the confidence our shareholders have in our future potential.

In addition to being recognised by investors, we received a research and development tax refund of $6.54m as part of the Australian government's R&D tax incentive for research activities undertaken during the financial year ended 30 June 2021. These refunds provide very important capital for the life sciences community in Australia and highlight the importance of our work as recognised by our Government. The receipt of the $6.54m in additional funding will be put to good use to further support our commercial and clinical milestones.

It was a pleasure to see many of you virtually attend our Annual General Meeting on 19 November 2021, and very satisfying to be able to provide you with a recap of the year past and talk about our plans for this year. We are well poised for an incredibly successful 2022 and we look forward to keeping you updated of our progress via the ASX and our electronic channels.

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.

Contact

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Connect

imugene.com

Financial Snapshot as at 30 June 2022

ASX code	**IMU**
Market cap	**$1.09B**
52 week high/low	**$0.625 / $0.13**
Cash balance	**$109M (31 Mar 2022)**
Industry	**Biotechnology**

Note: All figures are in Australian dollars. Market capitalisation calculations based on ordinary shares (5.866b) only and excludes the dilutive impact of options outstanding (0.368b).

Top 5 Shareholders

Paul Hopper	**6.96%**
HSBC Custody Nominees Australia	**5.98%**
Richard Mann and Assoc.	**5.35%**
JP Morgan Nominees Australia Pty Limited	**4.57%**
Citicorp Nominees Pty Limited	**3.67%**