IMUGENE

Developing Cancer Immunotherapies

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AZER-CEL HITS MAJOR MILESTONE IN PHASE 1B CAR T TRIAL

December 2023

IMUGENE IS WELL POSITIONED TO CONTINUE TO DELIVER FURTHER KEY NEWSFLOW & MILESTONES

Leslie Chong
Imugene CEO & Managing Director

CEO UPDATE

I'm pleased to bring you our final newsletter of 2023, reflecting on another period of highly significant progress at Imugene. Our journey over the past few months has been marked by several important advancements, ultimately bringing us closer to our goal of revolutionising cancer treatment.

Positive early data and Fast Track Designation for VAXINIA

Our Phase 1 CF33-hNIS (VAXINIA) MAST study has been our headline act recently, showing promising early results, particularly in patients with challenging gastrointestinal cancers. This paved the way for our receipt of Fast Track designation awarded by the FDA for VAXINIA, underscoring its potential in addressing the urgent treatment need for bile duct cancer.

This designation significantly streamlines the development and review process, enabling more frequent and strategic discussions with the FDA regarding VAXINIA's development plan.

It opens avenues for Accelerated Approval and Priority Review if certain criteria are met and supports a Rolling Review for our New Drug Application or Biologic License Application. We remain pleased by the progress of the multicentre Phase 1 MAST trial as it continues to successfully clear the various cohorts and arms in the study.

Azer-cel hits Phase 1b initiation milestone

Following our acquisition of the technology in August, we've seen strong progress in our azer-cel program. The initiation of the Phase 1b clinical trial, with the first patient being dosed, marks a step forward in evaluating this promising therapy for non-Hodgkin's lymphoma, especially Diffuse-Large B-cell lymphoma. The Phase 1a trial's findings, involving multiple US centres, laid a foundation for further exploration of azer-cel's safety and efficacy. Our goal for 2024 includes potentially initiating a Phase 2 registrational study, subject to FDA agreement, which could help us understand azer-cel's broader impact in cancer treatment. Additionally, we are continuing to explore opportunities to integrate azer-cel with our onCARlytics platform for solid tumour treatments, which aligns with Imugene's strategic vision for comprehensive cancer care.

Initiation of onCARlytics CD19 Virus Technology Trial

Entering the clinic for the first time, the initiation of our Phase 1 clinical trial for CD19 oncolytic virotherapy onCARlytics was another major piece of news. This trial represents a novel approach to treating solid tumours, combining our innovative therapy with approved CD19 drugs. The world-first clinical trial of a CD19 oncolytic virus in combination with a CD19 drug opens new treatment avenues for patients with solid tumours, historically challenging to treat with CD19-targeting biological drugs.

Outlook for 2024

Looking ahead to 2024, Imugene is well positioned to continue to deliver further key newsflow and milestones with five clinical studies ongoing. A critical focus will be advancing azer-cel through its clinical trials, with the aim of initiating a Phase 2 registrational study. This move is pivotal, as it could position azer-cel as the potential first approved allogeneic CAR T cell therapy for cancer, a remarkable achievement in our industry.

We're eager to see what the onCARlytics Phase 1 program delivers, both in the recently initiated clinical trial as well as the synergistic potential with azer-cel in treating solid tumours, thus broadening our impact across the oncology spectrum. The progress in the now expanded MAST study, buoyed by Fast Track designation, will be crucial as we expedite our clinical program.

We also anticipate fostering closer cooperation with regulatory bodies and exploring new partnerships to expand our reach and enhance our capabilities. Financially, our balance sheet remains strong, and we remain well funded to continue the advancement of our ongoing programs. As always, our strategy will be guided by our commitment to making a tangible difference in the lives of cancer patients worldwide.

On behalf of the Imugene team I wish you and your families a safe and happy holiday season and new year.

Q&A WITH IMUGENE'S CMO DR PAUL WOODARD

Please tell us about your experience prior to joining Imugene?

I was trained as a pediatric oncologist and stem cell transplanter and practiced for about a dozen years. I was a faculty member and eventually Vice Chair of the Clinical Staff at St. Jude Children's Research Hospital. After that, I joined the biotech/pharma industry in 2007. I first worked in medical affairs at PDL Biopharma, then transitioned to clinical development roles with increasing responsibility at Exelixis (where I met Leslie and Ursula), Amgen, Genentech, Bellicum, Immune-Onc, and now Imugene. I have had the opportunity to work on a variety of different small molecules, antibodies, including immunotherapies and CARTs. Some of those are now commercially available treatments for patients.

What appealed to you about Imugene?

A combination of the team Leslie had assembled and the innovative pipeline. Things like azer-cel and onCARlytics have the potential to be game-changing therapies.

What does your role as CMO at Imugene involve?

I have oversight over all aspects of clinical development and research at Imugene. I get to see data as it comes in and work on ways to develop the next-generation versions of our therapies.

How do you spend your weekends, do you have any hobbies?

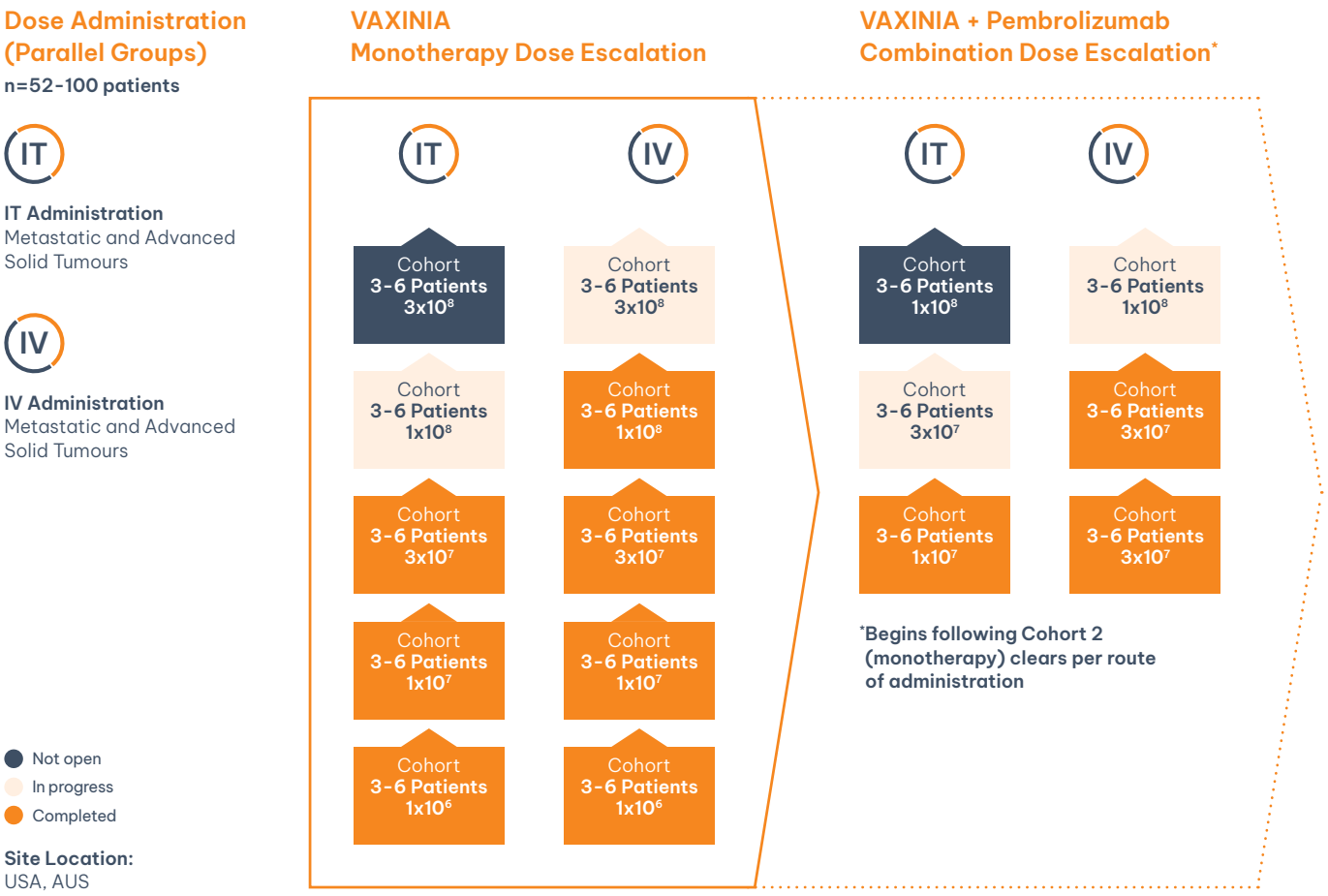
I enjoy cycling, reading and spending time with my family.

Where is your favourite travel destination and why?

It is hard to narrow it to just one! I love France and I love Sonoma County in California.

VAXINIA CONTINUES TO DELIVER POSITIVE EARLY DATA

FDA FAST TRACK FOR BILE DUCT CANCER



Also in November, we achieved notable progress in our Phase 1 CF33-hNIS (VAXINIA) Study, with positive early signals emerging from the trial. The study comprises VAXINIA alone or in combination with pembrolizumab, administered either intravenously (IV) or intratumourally (IT).

Up until the announcement of the early data, 34 heavily pre-treated patients had been dosed with CF33-hNIS virus, all of which have been determined safe and tolerable. Notably, one patient with bile duct cancer achieved a Complete Response (CR) in the mid dose on study for over 350 days, and another patient with melanoma showed a Partial Response (PR) at the mid dose. Additionally, 16 patients had Stable Disease (SD).

Also notable was that 7 patients with gastrointestinal cancers who received CF33-hNIS alone, including those with colorectal, bile duct, pancreatic, and liver cancers, showed positive treatment effects with a disease control rate (CR, PR, and SD combined) of 86%. Given the early results, the trial has been expanded with a further 10 patients with bile duct cancers to be enrolled.

Following these positive developments, we were pleased to announce that VAXINIA had been granted Fast Track designation for bile duct cancer by the US Food and Drug Administration (FDA).

The Fast Track designation facilitates a closer cooperation with the FDA to expedite the clinical program and subsequent potential approval process for VAXINIA. This includes benefits such as increased

frequency of meetings with the FDA to discuss the drug's development plan, eligibility for Accelerated Approval and Priority Review if relevant criteria are met, and a Rolling Review in support of a New Drug Application or Biologic License Application.

The multicentre Phase 1 MAST trial of VAXINIA commenced by delivering a low dose of the drug to patients with metastatic or advanced solid tumours who have had at least two prior lines of standard of care treatment. The City of Hope-developed oncolytic virus has shown promise in shrinking various cancer tumours in preclinical models.

The study has successfully cleared cohort 4 of the intravenous (IV) arm of the monotherapy dose escalation study and IV cohort 2 of the combination study where VAXINIA is administered with the checkpoint inhibitor drug pembrolizumab (KEYTRUDA®). With this progress, cohort 5 of the IV arm for the monotherapy dose escalation and IV cohort 3 of the combination study are now open.

AZER-CEL HITS MAJOR MILESTONE IN PHASE 1B CAR T TRIAL

In November, we achieved a significant milestone with the successful dosing of the first patient in the Phase 1b clinical trial of azer-cel, our innovative allogeneic off-the-shelf CD19 CAR T cell therapy.

This follows the promising results of the Phase 1 trial, which involved 84 patients across multiple U.S. Centres, marking an important advancement in our cancer treatment research. Azer-cel is being evaluated in a multi-centre Phase 1b clinical trial for patients with non-Hodgkin's lymphoma (NHL), focusing on those with Diffuse-Large B-cell lymphoma (DLBCL), a challenging subset of NHL.

The Phase 1 trial showed strong safety and efficacy signals, especially in DLBCL patients. Our aim is to initiate a Phase 2 registrational study in 2024, subject to FDA agreement, which could position azer-cel as a potential first approved allogeneic CAR T cell therapy for cancer.

The production of azer-cel is conducted in our state-of-the-art facility in North Carolina, ensuring high quality and effectiveness. Our strategic vision extends beyond blood cancers, with plans to combine azer-cel with our onCARlytics for the treatment of solid tumours, addressing a broader spectrum of the oncology market.

PHASE 1 CLINICAL TRIAL OPENS

WITH ONCARLYTICS CD19 VIRUS TECHNOLOGY

In October, we commenced our Phase 1 clinical trial for CD19 oncolytic virotherapy, onCARlytics at City of Hope in California and other US sites.

The first patient dosed in this innovative trial is being treated for ovarian cancer. The onCARlytics Phase 1 trial, known as OASIS, is focused on patients with solid tumours. The trial, titled "A Phase I Dose Escalation and Dose Expansion Safety and Tolerability Study of onCARlytics Administered Intravenously or Intratumourally in Combination with Blinatumomab in Adults with Advanced or Metastatic Solid Tumours," is designed to evaluate the safety and efficacy of onCARlytics administered through two methods: intratumoural (IT) injection and intravenous (IV) infusion, either alone or in combination with blinatumomab.

The therapy aims to make solid cancers susceptible to attack by approved CD19 drugs such as Amgen's Blincyto and Gilead's Yescarta, and potentially Imugene's future product, azer-cel.

This initiation of a world-first clinical trial of a CD19 oncolytic virus in combination with a CD19 drug offers a new avenue of treatment for patients with solid tumours, which have historically been challenging to treat with CD19-targeting biological drugs.

NEW PD1-VAXX PHASE 2 TRIAL TO TARGET COLORECTAL CANCER

Most recently, Imugene announced that in collaboration with the University of Southampton, Cancer Research UK Southampton Clinical Trials Unit at the Royal Surrey Hospital NHS Foundation Trust and The Australasian Gastro-Intestinal Trials Group (AGITG), it would open a Phase 2 clinical trial, "Neo-POLEM", in which the PD1-Vaxx vaccine will be evaluated for patients diagnosed with operable colorectal cancer.

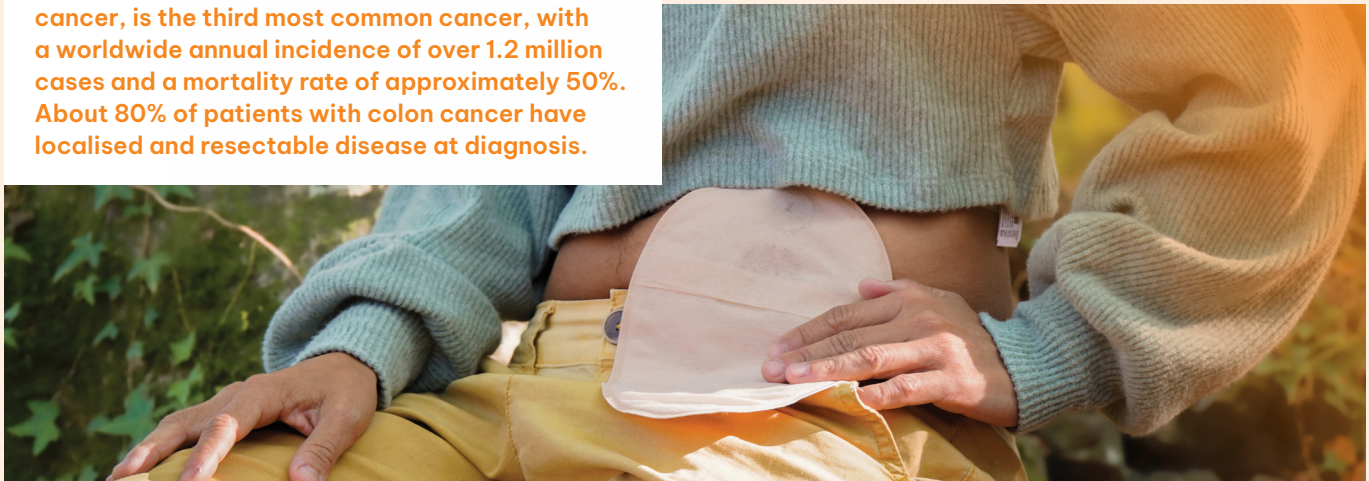
The title of the study is "A phase 2 trial of neoadjuvant PD-1 vaccine IMU-201 (PD1-Vaxx) in operable dMMR/MSI-H Colorectal Cancer". The primary objective of the study is to determine the pathological response rates and the secondary objectives are to assess the safety of PD1-Vaxx, evaluate biomarkers, and evaluate the objective response rates and overall survival.

Imugene also announced the European Patent Office issued a notification of Intention to Grant a patent for PD1-Vaxx.

The patent application, which covers the manufacturing and method of treatment, is expected to proceed to grant in late 2023 following completion of the grant formalities. Once granted, the patent will have a maximum term that will expire on 28 March 2038. The European Application (number 3600398) is titled "HUMAN PD1 PEPTIDE VACCINES AND USES THEREOF".

Corresponding applications are pending in Canada, China, Hong Kong, India, South Korea, Brazil and Australia. The patent has previously received a Notice of Grant in the US and Japan.

Colorectal cancer, also known as bowel cancer, is the third most common cancer, with a worldwide annual incidence of over 1.2 million cases and a mortality rate of approximately 50%. About 80% of patients with colon cancer have localised and resectable disease at diagnosis.



FEATURED AT ESMO CONGRESS

IMUGENE'S B CELL IMMUNOTHERAPY & ONCOLYTIC VIROTHERAPY PLATFORMS

Our B cell immunotherapy HER-Vaxx and CF33 oncolytic virotherapy CHECKVacc were prominently featured at the European Society for Medical Oncology (ESMO) Congress held in Madrid.

This event is highly influential in the field of oncology, bringing together clinicians, researchers, patient advocates, journalists, and healthcare industry representatives from around the globe.

At the congress, several presentations highlighted the progress and findings related to Imugene's innovative therapies. Key among them was the poster on the HERIZON Phase 2 study of HER-Vaxx (IMU-131), a HER2-targeting peptide vaccine combined with standard of care chemotherapy for patients with HER2+ advanced stomach cancer. The study showcased dose-dependent anti-cancer antibodies correlating with improved clinical outcomes. Furthermore, the efficacy of HER-Vaxx in generating robust anti-HER2 antibody responses was highlighted, validating its mechanism of action in overexpressing gastric cancer.

Another presentation focused on the preventive role of combination therapy targeting HER2 and PD-L1 in HER2-expressing tumours, based on efficacious vaccination against HER2-positive tumours observed in both preclinical and clinical settings. This research indicates that targeting HER2 induces upregulation of PD-L1, suggesting a potential clinical synergy in treating metastatic HER2+ cancers and preventing new metastasis development and immune evasion.

Additionally, the congress featured a poster on the induction of an inflammatory tumour microenvironment with oncolytic virus CF33-hNIS-antiPD-L1 intratumoural injection in patients with metastatic triple negative breast cancer (mTNBC). The findings highlighted the safety and tolerability of the treatment, its role in inducing tumour infiltration of critical immune cells, and significant upregulation of PD-L1 within the tumour microenvironment.

INVESTOR ROADSHOW WITH IMUGENE EXECUTIVE TEAM

During November, Imugene was pleased to welcome its US-based COO Dr Bradley Glover and CMO Dr Paul Woodard to Australia to present as part of a non-deal roadshow.

Alongside Managing Director and CEO Leslie Chong, the executive team delivered presentations to investors and shareholders at well attended events in Sydney, Melbourne and Adelaide.

The team also conducted a webinar for all other shareholders and interested parties, speaking to the same presentation and information.

A replay can be viewed at:

https://youtu.be/BoLoplUXRm8?si=CwTTxMJcuohkLPII

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FROM THE CHAIR

While it's been only a short time since our last newsletter, it's pleasing to be able to write this update after a period of such important and well received news flow about our clinical progress.

To have in two months seen the first patient dosed for both the azer-cel Phase 1b and onCARlytics Phase 1 trials, as well as be able to announce such encouraging preliminary data from the VAXINIA MAST study, is again a credit to our hard-working team and high-quality science.

I want to express my gratitude for your support during our recent Annual General Meeting. Your overwhelming support of the board and management with approval of all resolutions presented, is a testament to the trust you place in us at Imugene.

We appreciate your support of the corporate direction of the company and reinforces our target to achieving our clinical goals and driving sustained value for shareholders and positive outcomes for patients in need.

Looking ahead, I feel your company is well positioned as it enters 2024. As we approach the holiday season, I would like to take this opportunity to extend my warmest wishes to you and your families.

Thank you once again for your continued support. We look forward to a successful and promising 2024.

Paul Hopper
Executive Chairman

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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Connect

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Financial Snapshot as at 5 December 2023

ASX code	IMU
Market cap	$666m
52 week high/low	$0.20 / $0.039
Cash balance	$163m (30 September 2023)
Industry	Biotechnology

Note: All figures are in Australian dollars. Market capitalisation calculations based on ordinary shares (7.165b) only and excludes the dilutive impact of options outstanding (0.479b).

Top 5 Shareholders

Mr Paul Hopper	4.47%
Mann Family	4.03%
The Vanguard Group, Inc	3.60%
Dr Nicholas Smith	1.65%
UBS Group AG	1.49%