Imugene Highlights Recent Achievements and Looks Ahead to Key Upcoming Immuno-oncology Catalysts

- Five clinical trials across three prioritized immuno-oncology platforms with encouraging safety and efficacy signals
- Encouraging early results from the VAXINIA (CF33) oncolytic virus trial, including one complete response in a patient with cholangiocarcinoma (bile tract cancer) and two partial responses in patients with melanoma; two out of three of the responses were achieved with monotherapy CF33; receipt of US FDA Fast Track Designation for bile duct cancer
- Potential near-term registrational study and fast-to-market strategy for azer-cel allogeneic CAR T therapy in patients with relapsed/refractory diffuse large B cell lymphoma (DLBCL) who progressed after autologous CAR T therapies
- World-first onCARlytics trial designed to convert "targetless" tumors to CD19-expressing solid tumors that are otherwise hard to treat; trial combines a CD19-expressing oncolytic virus with a CD19 targeting drug

Sydney, Australia, 22 February 2024: Imugene Limited (ASX: IMU), a clinical stage immuno-oncology company, highlighted recent progress across the company's immuno-oncology portfolio and provided an update on anticipated upcoming milestones.

Imugene Managing Director & CEO Leslie Chong said: "We are encouraged by the initial safety and efficacy signals seen to date. Notably, in our Phase 1 MAST CF33 oncolytic virus trial, we've seen encouraging response rates during dose escalation, including one complete response in a patient with cholangiocarcinoma, and two partial responses in melanoma as we continue to dose escalate with no safety issues. Importantly, two out of three of these responses were achieved with CF33 monotherapy. In addition, we have seen encouraging response rates with azer-cel, our allogeneic CAR T cell therapy for patients with diffuse large B cell lymphoma who have failed auto CAR T treatments, and we look ahead to a potential registrational trial."

Ms. Chong continued: "In addition, we continue to advance our novel onCARlytics combination immunotherapy program that, in simple terms, a mark-and-kill approach. onCARlytics uses an antigen/target-armed CF33, followed by treatment with a CD19 targeting therapy directed against that

antigen or target. We believe onCARlytics may provide a new solution for clinicians to treat previously untreatable solid tumours."

Program Highlights

Oncolytic virus (CF33) - *a chimeric vaccinia (pox) virus known as CF33 that has the potential to act as both a target delivery vehicle and an oncolytic agent.*

- The engineered CF33 virus selectively replicates itself in tumor cells, causing the cell to rupture, releasing new virus particles capable of infecting other tumor cells
- CF33 has demonstrated multiple ways to kill cancer cells: by direct killing, by the activation of immune cells to kill cancer cells, and by priming the tumor environment to enhance the immune response; CF33 has been shown to turn cold tumors hot
- The Phase 1 MAST trial assesses the safety and efficacy of CF33 administered alone, or in combination with pembrolizumab and either dosed intravenously (IV) or intratumourally (IT)
- As of January 2024, 34 heavily pre-treated patients had been dosed with VAXINIA
- Data presented at ASCO-GI in January demonstrated the following:
    - 31 patients were evaluable for efficacy
    - Response rates seen during dose escalation at doses lower than the current dose
        - In the IT cohorts (14 patients), 7 of 15 (47%) injected lesions had a reduction in tumor burden, 3 lesions were completely eradicated
        - 3 patients (21%) had an objective response:
            - 1 monotherapy complete response (CR) by iRECIST in a patient with cholangiocarcinoma who previously failed three lines of chemotherapy; the patient has been in remission for over a year and half
            - 2 partial responses in patients with melanoma (skin cancer) by RECIST, one with monotherapy and one in combination with pembrolizumab.
        - In IV cohorts (17 patients), 53% of patients achieved stable disease as their best response
    - All treatments to date have been determined safe and tolerable
- The company received US FDA Fast Track Designation for bile duct cancer in November 2023
- Expansion of cholangiocarcinoma and other indications are planned for 2024

- Biliary tract cancer, also known as cholangiocarcinoma, is a rare but aggressive malignancy that originates in the bile ducts
- The highest incidence is in South East Asia with incidence (0.3–6 per 100,000 inhabitants per year) and mortality (1–6 per 100,000 inhabitants per year, globally, not taking into account specific regions with incidence >6 per 100,000 habitants such as South Korea, China and Thailand) have been increasing in the past few decades worldwide, representing a global health problem.[1]
- The U.S. accounted for 10,064 total incident cases of BTC in the year 2023, which is expected to increase at a moderate rate[2]

Azer-cel: *allogeneic (off-the-shelf) CAR T cell therapy targeting CD19 for the treatment of hematological malignancies.*

- Allogeneic, or off-the-shelf, CAR T-cell therapy, uses T cells from healthy donors, making the treatment immediately available to patients, more potent, and less expensive than current approved autologous CAR T treatments
- Ongoing Phase 1b clinical trial in patients with non-Hodgkin's lymphoma (NHL) who relapsed following autologous CAR T therapy
- Data from prior Phase 1 azer-cel trial demonstrated clinically meaningful activity with an acceptable safety profile in 84 patients across leading US centres. Results from 18 patients with DLBCL who relapsed from prior autologous CAR T showed:
    - 83% Overall Response Rate (ORR)
    - 61% Complete Response (CR)
    - 55% of patients achieving durable responses greater than or equal to six months in patients with DLBCL who had relapsed following auto CAR T therapy (n=18)
- Positive FDA guidance on the potential registrational study, which could start after completion of the confirmation study; if successful, azer-cel has the potential to become the first approved allogeneic CAR T cell therapy for cancer
- DLBCL is the most common type of NHL, with approximately 80,500 cases per year[3] and approximately 30,000 new cases per year in the U.S.
- Relapsed/refractory DLBCL has a high unmet medical need; 60-65% of patients treated with autologous CD19 CAR T relapse

onCARlytics (CF33-CD19) – *A novel engineered oncolytic virus (CF33) that can deliver a CD19 target to "targetless" solid tumors that are otherwise hard to treat*

- onCARlytics is a CD19-expressing oncolytic virus that enters tumor cells and forces them to express the CD19 protein on the cell surface, presenting a target for CD19 targeting therapies
- Solid cancers like breast, lung, gastric, and colon, etc. don't have a common target such as CD19 on their cell surface; the goal of onCARlytics is to present a target for CD19 therapies
- Solid tumors make up 90 percent of the cancer market; if successful onCARlytics could make CD19 therapy an option to treat patients with solid tumors
- The Phase 1 OASIS trial is a world-first in combining a CD19-expressing oncolytic virus with CD19 targeted therapy (blinatumomab, Blincyto®)
- The primary objective of the trial is to evaluate the safety and efficacy of onCARlytics, either by intratumoural (IT) injection or intravenous (IV) infusion, either alone, or in combination with blinatumomab, in approximately 52 adult patients with advanced or metastatic solid tumors
- The first patient in the monotherapy IT arm was dosed in October 2023; the first patient in the monotherapy IV arm was dosed in February 2024
- The next step is to combine onCARlytics with azer-cel allogeneic CAR T therapy, a combination strategy that has shown preclinical proof-of-principle

*iRECIST and RECIST: (immune) Response evaluation criteria in solid tumors

*PFU: Plaque Forming Unit

References:;

[1]*Banales, J.M., Marin, J.J.G., Lamarca, A. et al. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. Nat Rev Gastroenterol Hepatol 17, 557–588 (2020). https://doi.org/10.1038/s41575-020-0310-z*

[2]*DelveInsight Business Research LLP Biliary Tract Cancers (BTCs) - Market Insight, Epidemiology And Market Forecast – 2032*

[3]*NIH National Library of Medicine, PDQ Cancer Information Summaries, May 18, 2023*

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About Imugene (ASX:IMU)

Imugene is a clinical stage immuno-oncology company developing a range of new and novel immunotherapies that seek to activate the immune system of cancer patients to treat and eradicate tumours. Our unique platform technologies seek to harness the body's immune system against tumours, potentially achieving a similar or greater effect than synthetically manufactured monoclonal antibody and other immunotherapies. Our pipeline includes an off-the-shelf (allogeneic) cell therapy CAR T drug azer-cel (azercabtagene zapreleucel) which targets CD19 to treat blood cancers. Our pipeline also includes multiple immunotherapy B-cell vaccine candidates and an oncolytic virotherapy (CF33) aimed at treating a variety of cancers in combination with standard of care drugs and emerging immunotherapies such as CAR T's for solid tumours. We are supported by a leading team of international cancer experts with extensive experience in developing new cancer therapies with many approved for sale and marketing for global markets.

Our vision is to help transform and improve the treatment of cancer and the lives of the millions of patients who need effective treatments. This vision is backed by a growing body of clinical evidence and peer-reviewed research. Imugene is well funded and resourced, to deliver on its commercial and clinical milestones. Together with leading specialists and medical professionals, we believe Imugene's immuno-oncology therapies will become foundation treatments for cancer. Our goal is to ensure that Imugene and its shareholders are at the forefront of this rapidly growing global market.