IMUGENE
Developing Cancer Immunotherapies

ASX Announcement

Phase 1 CF33-hNIS (VAXINIA) Study Update

Positive Early Signals

- **The study structure comprises of CF33-hNIS alone, or in combination with pembrolizumab and either dosed intravenously (IV) or intratumorally (IT)**
- **34 heavily pre-treated patients dosed to date with CF33-hNIS virus**
- **All treatments to date have been determined safe and tolerable**
- **One Complete Response (CR)* in bile duct cancer in the mid dose on study for over 350 days**
- **One Partial Response (PR)* in melanoma in the mid dose**
- **16 patients had Stable Disease (SD)***
- **7 patients with gastrointestinal cancers who received CF33-hNIS alone including 3 colorectal cancer, 2 bile duct,1 pancreatic and 1 liver cancer showed positive treatment effects, with a disease control rate (all CR, PR and SD) of 86%**

Sydney, Australia, 6 November 2023: Imugene Limited (ASX: IMU), a clinical stage immuno-oncology company, is pleased to provide a clinical trial update of its Phase 1 MAST (Metastatic Advanced Solid Tumours) trial evaluating the safety and efficacy of novel cancer-killing virus CF33-hNIS (VAXINIA).

As announced last week, the trial has now cleared cohort 4 of the intravenous (IV) arm of the monotherapy dose escalation study, as well as IV cohort 2 of the combination study where VAXINIA is administered with checkpoint inhibitor drug pembrolizumab (KEYTRUDA®). Cohort 5 of the IV arm for the monotherapy dose escalation is now open as is IV cohort 3 of the combination study.

- As of 31 October 2023, 34 patients have been dosed with VAXINIA during the continuing dose escalation phase comprised of 16 patients intratumorally and 18 patients intravenously as either monotherapy or in combination with

pembrolizumab. Twenty-five patients were evaluable (received at least their first scan at day 42) and seven patients have their first scan still pending. Of the evaluable patients the BOR (best overall response) are 1 Complete Response (CR), 1 Partial Response (PR), 16 Stable Disease (SD), showing patients had control and stability of their cancer and 8 progressive disease (PD) as measured by iRECIST* and RECIST* criteria

- Importantly early results from 6 patients with gastrointestinal cancers who received CF33-hNIS alone including 2 colorectal cancer, 2 bile duct, 1 pancreatic and 1 liver cancer showed positive treatment effects, with a disease control rate (all CR, PR and SD) of 75%
- Trial expansion is planned for 10 patients with bile duct cancers

Imugene MD & CEO Leslie Chong said: "Phase 1 trials are generally designed to look for safety, tolerability and early response signals to determine the optimal dose for further development. The early positive response data we are seeing at the mid-dose level in hard-to-treat bile duct cancer suggests that VAXINIA may be a potent anti-cancer drug as we interrogate higher dose levels. With no adverse safety signals, thus allowing us to dose higher, VAXINIA will have a very high therapeutic window which is valuable in oncology drug development."

Notably one patient with bile duct cancer, treated IT with mid-dose level displayed pseudoprogression (see below) with a 49% increase in tumour burden after two cycles of therapy. However, by the 4th cycle they achieved a Complete Response (iCR) with no known recurrence in over 200 days. A second patient with bile duct cancer, who previously progressed on prior drug therapies, achieved Stable Disease (SD) for > 4 months upon receiving IV-administered CF33-hNIS.

Bile duct cancers are difficult to treat and typically respond poorly to immunotherapy drugs. Pseudoprogression is a phenomenon in which the cancer initially appears to be growing, largely due to the cancer cells being infected by the virus then followed by infiltration of cancer fighting immune cells. However, it is usually followed by a decrease in tumour burden when the therapy takes effect. This phenomenon can benefit patients

receiving immunotherapy but often leads to premature discontinuation of treatment owing to the false impression the cancer is growing.

The multicenter Phase 1 MAST trial commenced by delivering a low dose of VAXINIA 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 been shown to shrink colon, lung, breast, ovarian and pancreatic cancer tumours in preclinical laboratory and animal models[1]. Overall, the study aims to recruit cancer patients across approximately 10 trial sites in the United States and Australia.

The clinical trial is titled "A Phase I, Dose Escalation Safety and Tolerability Study of VAXINIA (CF33- hNIS), Administered Intratumorally or Intravenously as a Monotherapy or in Combination with Pembrolizumab in Adult Patients with Metastatic or Advanced Solid Tumours (MAST)." The trial commenced in May 2022 and is anticipated to run for approximately 24 months while being funded from existing budgets and resources.

Full study details can also be found on clinicaltrials.gov under study ID: NCT05346484.

*iRECIST and RECIST: (immune) Response evaluation criteria in solid tumours
*PFU: Plaque Forming Unit

References

[1] Warner SG, Kim SI, Chaurasiya S, O'Leary MP, Lu J, Sivanandam V, Woo Y, Chen NG, Fong Y. A Novel Chimeric Poxvirus Encoding hNIS Is Tumor-Tropic, Imageable, and Synergistic with Radioiodine to Sustain Colon Cancer Regression. Mol Ther Oncolytics. 2019 Apr 11;13:82-92. doi: 10.1016/j.omto.2019.04.001. PMID: 31061881; PMCID: PMC6495072.

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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.

Release authorised by the Managing Director and Chief Executive Officer Imugene Limited.