ASX Announcement

Update on Phase I Clinical Trial of Oncolytic Virotherapy CHECKvacc

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SYDNEY, Australia, 7 December 2021: Imugene Limited (ASX:IMU), a clinical stage immuno-oncology company, today announced that City of Hope®, a world-renowned independent cancer research and treatment center near Los Angeles, has dosed the second patient in the Phase I clinical trial of oncolytic virotherapy candidate, CHECKvacc (CF33-hNIS-antiPDL1). This follows the first patient (as announced on 20 October 2021) clearing the 28-day safety window between patient dosing in the initial cohort, as instructed by the FDA.

The first-in-human, Phase 1, single-centre, dose escalation study of CHECKvacc is recruiting patients with triple negative breast cancer (TNBC). The purpose of the study is to evaluate the safety and initial evidence of efficacy of intratumoural administration of CF33-hNIS-antiPDL1 against metastatic TNBC. The current trial design will involve a dose escalation, followed by an expansion to 12 patients at the final dose, which will be the recommended phase 2 dose (RP2D).

The clinical trial is titled "A Phase I Study of Intratumoural Administration of CF33-hNIS-antiPDL1 in Patients with Advanced or Metastatic Triple Negative Breast Cancer". The Principal Investigator leading the trial is Dr Yuan Yuan MD, PhD.

CF33-hNIS-antiPDL1 is an immune checkpoint inhibitor armed chimeric vaccinia poxvirus from the lab of CF33 inventor Professor Yuman Fong, Chair of Sangiacomo Family Chair in Surgical Oncology at City of Hope, and a noted expert in the oncolytic virus field.

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.

Imugene MD & CEO Leslie Chong said: "As this is our first Oncolytic Virotherapy in the clinic, it's great to have no safety issues thus far with our first patient and we are very pleased to see our second patient joining the trial immediately following the FDA specified 28-day stagger between patient dosing. We hope that in time, CHECKvacc provides an improved outcome for the many women who are diagnosed every year with TNBC. We look forward to seeing the results of this trial and bringing continued updates to the medical community and our stakeholders moving forward."

Full study details can also be found on clinical trials.gov under study ID: NCT05081492.

For more information please contact:

Leslie Chong
Managing Director and Chief Executive Officer
info@imugene.com

Investor Enquiries
investor@imugene.com

Media Enquiries
Matt Wright
matt@nwrcommunications.com.au

Follow us on Twitter @TeamImugene
Like us on Facebook @Imugene
Connect with us on LinkedIn @Imugene Limited

About Triple-Negative Breast Cancer

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer (affecting about 20% of all breast cancer patients), characterized by the lack of expression of estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2), with a dismal median survival of 12 months. There is no effective targeted therapy in patients with metastatic TNBC with the exception of tumours with germline BRCA mutation, which highlights TNBC as an area of unmet need. Moreover, TNBC rapidly develops resistance to chemotherapy, and thus advances in chemotherapy alone are unlikely to improve prognosis. Therefore, novel therapies are desperately needed to improve the clinical outcome of TNBC.

About CHECKvacc

CF33-hNIS-antiPDL1 (CHECKvacc) is a novel chimeric orthopoxvirus with robust anti-cancer activity including TNBC xenografts. Cells infected with CF33-hNIS-antiPDL1 were shown to express functional hNIS and anti-PD-L1 proteins. hNIS gene transfer allows tracking of virus by non-invasive imaging as well as radioiodine therapy. City of Hope's preliminary animal studies demonstrated that tumour cells infected with CF33-hNIS-anti-PD-L1 successfully secrete functional hNIS and immune checkpoint inhibitor anti-PD-L1. CF33-hNIS-antiPDL1 is safe and well-tolerated, detects and effectively kills TNBC at doses several magnitudes lower than other oncolytic viruses currently under clinical testing.

Extensive studies of CF33-hNIS-antiPDL1 have been perform on TNBC cancer cells in tissue culture. As few as 1 viral particle per 1000 tumour cells can kill all cell lines tested by 2 weeks. In very susceptible cell lines, complete cancer cell killing can occur within 1 week. Such effective cancer cell killing has also

been observed for pancreatic cancer cells, stomach cancer cells, lung cancer cells, ovarian cancer cells and brain cancer cells in tissue culture.

Extensive testing in mice with TNBC as well as other cancer have been undertaken. Administration of CF33-hNIS-antiPDL1 allows for visualization of viral distribution in animals by non-invasive imaging. Administration of CF33-hNIS-antiPDL1 recruits cancer killing lymphocytes to areas with cancer. These effects can be seen at doses producing few side-effects in mice.

About the Trial

Full study details can also be found on clinical trials.gov under study ID: NCT05081492.

This phase I trial tests the safety, side effects, and best dose of CF33-hNIS-antiPDL1 in treating patients with triple negative breast cancer that has spread to other places in the body (metastatic). CF33-hNIS-antiPDL1 is an oncolytic virus. This is a virus that is designed to infect tumour cells and break them down.

PRIMARY OBJECTIVE:

1. To determine the safety and tolerability of a novel chimeric oncolytic orthopoxvirus, oncolytic virus CF33-expressing hNIS/Anti-PD-L1 antibody (CF33-hNIS-antiPDL1), by the evaluation of toxicities including: type, frequency, severity, attribution, time course, reversibility and duration according to Common Terminology Criteria for Adverse Events (CTCAE) 5.0 criteria.

SECONDARY OBJECTIVES:

1. To determine the optimal biologic dose (OBD) (defined as a safe dose that induces an immune response in tumours [increase checkpoint target PD-L1 by at least 5% and/or increase T cell infiltration by at least 10%]) and the recommended phase II dose (RP2D) for future expansion trial.
2. To determine tumour response rates by Response Evaluation Criteria in Solid Tumours (RECIST) version (v)1.1 (primary) and immune-modified (i)RECIST (secondary).
3. To document possible therapeutic efficacy and evaluate progression-free survival, overall survival and response.

EXPLORATORY OBJECTIVE:

1. To determine the immune and genomic profiles of tumours before and after CF33-hNIS-antiPDL1 therapy.

Study Design: This is a dose-escalation study. Patients receive CF33-hNIS-antiPDL1 intratumourally (IT) on days 1 and 15. Treatment repeats every 28 days for up to 3 cycles in the absence of disease

progression or unacceptable toxicity. After completion of study treatment, patients are followed up at 30 days, then every 3 months for 1 year.

About Dr Yuan Yuan

Yuan Yuan, M.D., Ph.D. is an Associate Professor specializing in breast oncology in the Department of Medical Oncology & Therapeutics. Prior to joining City of Hope in 2012, she was an assistant professor at Loma Linda University Medical Center in the Division of Medical Oncology and Hematology, and a principal investigator for multiple breast cancer trials. Dr. Yuan received her Bachelor of Medicine degree from Xuzhou Medical College in Xuzhou, China, and an M.S. in oncology from Peking Union Medical College in Beijing, China. She went on to complete a Ph.D. in biochemistry and molecular biology from the University of California, Riverside. She then completed a research fellowship at the Scripps Research Institute in La Jolla, CA, followed by an internship and residency in internal medicine at the New York University Downtown Hospital in New York, NY. She furthered her training with a hematology and oncology fellowship at the New York University Medical Center, under the direction of Dr. Franco Muggia. Dr. Yuan's clinical research interests center on novel therapeutics for metastatic triple negative breast cancer (TNBC). She currently leads multiple clinical trials for metastatic triple negative breast cancer including the following targeted therapies: immune check point inhibitors, androgen receptor targeted therapy, PIK3CA pathway inhibition. She is awarded a STOP CANCER Career Development Award supporting translational research in TNBC tumour evolution and a NIH R03 grant studying biomarkers predicting chemotherapy toxicity in women with breast cancer undergoing chemotherapy. She is experienced in pre-clinical, translational, and clinical application of novel combination therapies. She has worked closely with City of Hope's translational scientist, molecular pathology core, genomics, bioinformatics and biostatistics core to study the longitudinal genomic mutation profiling of paired metastatic breast cancer. She serves as principal investigator for multiple investigator-initiated trials including a phase II trial combining letrozole, palbociclib and pembrolizumab in patients with HR+ 4 metastatic BC (NCT02778685); a phase I/IB clinical trial studying eribulin plus everolimus in patients with metastatic TNBC (NCT02120469); a phase II trial androgen receptor (AR) targeted therapy GTx-024 in combination with pembrolizumab in patients with metastatic AR+ TNBC; a phase IB study combining ipatasertib with carboplatin or carboplatin/paclitaxel in patients with metastatic TNBC. Her clinical trial work in AR+ TNBC was awarded Phase I Foundation Grant in correlative studies. Dr. Yuan has multiple publications in peer-reviewed literature and has been invited to present at national and international meetings. She is board certified in internal medicine, hematology and oncology

About City of Hope®

City of Hope is an independent biomedical research and treatment center for cancer, diabetes and other life-threatening diseases. Founded in 1913, City of Hope is a leader in bone marrow

transplantation and immunotherapy such as CAR T cell therapy. City of Hope's translational research and personalized treatment protocols advance care throughout the world. Human synthetic insulin, monoclonal antibodies, and numerous breakthrough cancer drugs are based on technology developed at the institution. Translational Genomics Research Institute (TGen) became a part of City of Hope in 2016. AccessHope™, a wholly owned subsidiary, was launched in 2019, dedicated to serving employers and their health care partners by providing access to City of Hope's exceptional cancer expertise. A National Cancer Institute designated comprehensive cancer center and a founding member of the National Comprehensive Cancer 5 Network, City of Hope is ranked among the nation's "Best Hospitals" in cancer by U.S. News & World Report. Its main campus is located near Los Angeles, with additional locations throughout Southern California and in Arizona. For more information about City of Hope, follow us on Facebook, Twitter, YouTube or Instagram.

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 product pipeline 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, Level 3, 62 Lygon Street, Carlton, VIC, 3053, Australia