

City of Hope Researchers Receive Large US Department of Defense Grant to Study Imugene Oncolytic Virotherapy CF33 in Gastric Cancer

Sydney, Australia, 23 October 2019: Imugene Limited (ASX:IMU) a clinical stage immuno-oncology company today announced that prominent City of Hope researchers Yanghee Woo, MD, Associate Clinical Professor, Department of Surgery and Director, Gastroenterology Minimally Invasive Therapy Program, together with Yuman Fong, MD, Professor and Chair of the Department of Surgery, received a \$564,173 US Department of Defense Grant titled “Discovery of Immune Biomarkers That Predict Response to a Novel Chimeric Immuno-Oncolytic Virus Encoding Anti-PD-L1 in Gastric Cancer Peritoneal Carcinomatosis”. City of Hope is a world-renowned independent research and treatment center for cancer, diabetes and other life-threatening diseases based near Los Angeles.

The grant focuses on the area of stomach (gastric) cancer (GC), a disease that disproportionately affects US military service members, veterans, and their beneficiaries who have increased exposure to hazardous environmental risk factors, such as *H. pylori*, Epstein-Barr viral infections, radiation, and tobacco smoking.

Peritoneal carcinomatosis (PC) is a fatal evolution of GC for which there is no effective treatment. Across military families and the general population, over 60% of all patients with GC will develop peritoneal disease as the most common manifestation of recurrence or metastatic presentation.

The progression of primary GC to PC is facilitated by the unique peritoneal tumor microenvironment, where metastatic peritoneal seeding requires evasion of anti-tumor immunity and maintenance of a highly immunosuppressive microenvironment. The researchers rationalize that a combined approach using Imugene’s proposed license for novel oncolytic virus CF33 armed to express an anti-PD-L1 antibody as immune modulator could specifically kill cancer cells, convert the immunologically ‘cold’ environment of PC into a ‘hot’ environment, and enhance overall efficacy of GC therapy.

Imugene’s M.D. & CEO, Ms Leslie Chong said “Imugene and City of Hope are committed to help improve the length and quality of life for patients with gastric cancer. We congratulate Dr. Yanghee Woo and Dr. Yuman Fong on receiving this sizable grant. It is an honour to work with the prestigious and prolific team at City of Hope to expand the development of CF33”.

IMU’s proposal to license CF33 from City of Hope is subject to a number of customary conditions precedent, and shareholder approval at the Extraordinary General Meeting (EGM) to be held on 18th of November, 2019.

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About Yanghee Woo, M.D.

Yanghee Woo, M.D., is a City of Hope surgeon-scientist specially trained and internationally recognized in robotic surgery and gastric cancer. She has particular expertise in complex procedures such as D2 lymphadenectomy for locally advanced gastric cancer. Dr. Woo offers her patients completely laparoscopic and robotic surgeries (for stomach and pancreas tumors) with optimal oncologic outcomes while preserving patients' quality of life. She is one of very few surgeons who treat gastric cancer and pancreatic cancer using minimally invasive methods.

In addition to her clinical practice, Dr. Woo is also actively researching better ways to detect, treat and prevent gastric cancer. This includes improving robotic and laparoscopic surgeries, enhancing early detection and prevention efforts in high-risk populations, and identifying biological, molecular and genetic markers that can lead to better treatment planning. As a translational member of the laboratory of Yuman Fong, M.D., she is part of the City of Hope team working to soon bring novel oncolytic viruses to our patients to cure cancer.

About Professor Yuman Fong, M.D.

A pioneer both in the operating room and in the laboratory, Professor Yuman Fong, M.D., The Sangiacomo Family Chair in Surgical Oncology and chair of City of Hope's Department of Surgery, is an internationally recognized expert in liver and pancreatic cancer. He has developed many new surgical techniques and instruments. He has also led research efforts to use genetically modified viruses to destroy cancer cells. Fong joined City of Hope in 2014 after more than two decades at the renowned Memorial SloanKettering Cancer Center in New York City. Fong is both an author and innovator. He has written and edited over 700 scholarly articles as well as 14 textbooks. He is currently the Editor-in-Chief of Molecular Therapy Oncolytics (Cell Press). Fong has had leadership roles in regulatory aspects of gene therapy, including serving as Chair of the Recombinant DNA Advisory Committee of the National Institutes of Health of the United States.

About the CF33 Oncolytic Chimeric Poxvirus

Oncolytic virotherapy (OV) utilizes naturally occurring or genetically modified viruses to infect, replicate in, and kill cancer cells, while sparing healthy cells. The first OV for human therapy was recently approved by the US Food and Drug Administration (FDA): T-VEC (talimogene laherparepvec, Amgen), for the treatment of

metastatic melanoma . Intriguingly, many cancer cell characteristics that lead to chemo- and radiation-resistance enhance the success of oncolytic virotherapy

C33 is a chimeric poxvirus derived through recombination among multiple strains of vaccinia virus and other species of poxvirus, thus it is better than a virus based on a single strain. One hundred chimeric orthopoxviruses and 100 chimeric parapoxviruses were generated.

Preclinical data has demonstrated that CF33 is more efficacious than all parental viruses and some viruses in clinical trials.

CF33 efficiently shrank injected tumours and distant non-injected tumours in human triple negative breast cancer, colon cancer, ovarian cancer xenograft models in mice without adverse effects at a dose that is 2-5 orders of magnitude lower than doses used for oncolytic viruses under clinical testing.

Especially impressive is that CF33 can shrink multiple types of cancer at an extremely low dose (1000 PFU). Importantly, CF33 shrinks not only injected tumours, but also non-injected distant tumours (abscopal effect).

CF33 showed superior replication and cancer cell killing in NCI-60 cell lines and is more potent than all the parental and competitor viruses in most of the NCI-60 cell lines except for a few cell lines in which none of the viruses showed any effect at the low MOI (0.01).

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 tumors. 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. 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.