IMUGENE
Developing Cancer Immunotherapies

ASX Announcement

onCARlytics virus combined with ARTEMIS® T cells demonstrate enhanced anti-tumour activity in primary liver cancer

Sydney, Australia, 18 May 2023: Imugene Limited (ASX: IMU), a clinical stage immuno-oncology company, is pleased to announce its onCARlytics technology, in combination with Eureka Therapeutics, Inc.'s ARTEMIS® cell receptor platform, has presented preclinical data at the American Society of Gene and Cell Therapy's Annual Meeting (ASGCT) demonstrating enhanced anti-tumour activity *in vivo* against hepatocellular carcinoma (liver cancer) tumours.

The data, presented as a poster presentation at the ASGCT conference held in Los Angeles, titled 'Effective combination immunotherapy using onCARlytics and ARTEMIS® CD19 T cells against hepatocellular carcinoma', investigates the combination in the most common type of primary liver cancer and sixth most common cancer worldwide.

Hepatocellular carcinoma (HCC) occurs most often in people with chronic liver diseases, such as cirrhosis caused by hepatitis B or hepatitis C infection.

Currently, there are few systemic therapies available for patients with advanced disease in addition to the traditional treatments including ablation, surgical resection, and liver transplantation. CD19-targeting chimeric antigen receptor (CAR) T cell therapy has demonstrated impressive clinical outcomes in blood cancers, but translating this therapy to solid-tumour cancers has met various challenges, including the immunosuppressive microenvironment, on-target off-tumour toxicity, and antigen heterogeneity. To date, CAR T cell therapies against HCC have shown nominal efficacy in clinical trials. Therefore, development of novel and innovative therapeutic approaches against HCC is needed to overcome the challenges and improve clinical outcomes.

onCARlytics in combination with ARTEMIS® T cells potentially provide a solution. ARTEMIS® T cells differentiate from CAR T cells with lower CRS risks, better tumour infiltration, and higher T cell persistence in pre-clinical studies, making them ideal cell therapy candidates for solid tumours.

The ASGCT event is now in its 26th year and attracts a range of professionals in the area of gene and cell therapy, who observe new scientific research and technologies alongside peers in the industry. It is being held 16-20 May 2023 at the Los Angeles Convention Center, CA, USA.

The poster presentation can be viewed on the Imugene website, https://www.imugene.com/conference-presentations.

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About the CF33 Oncolytic Virus Platform

Oncolytic virotherapy is an emerging, novel therapeutic approach for solid tumours that selectively replicates in and destroys tumour cells while leaving normal cells undamaged.

CF33 is a "chimeric poxvirus" derived through recombination among multiple strains of vaccinia virus strains, that has been engineered to be far superior to a virus based on a

single strain. CF33 efficiently shrinks injected tumours and distant non-injected tumours in human triple negative breast cancer, colon, ovarian, lung, pancreatic and liver cancer models in mice. This was demonstrated without adverse effects at a dose that is 2-5 orders of magnitude lower than doses used for oncolytic viruses under current clinical testing. As well as being able to shrink multiple types of cancers at an extremely low dose, CF33 importantly also shrinks non-injected distant tumours (abscopal effect).

Imugene is developing three forms of CF33, all of which contain an identical genetic sequence resulting in equal tumour targeting and killing potential.

CF33 is a modern-day cancer fighting soldier specifically trained to target and destroy tumour cells with precision. CF33 is armed with "specialised weapons" that either help detect the tumour (via marking the tumour with a target flag) or assist the immune system to complete the elimination of the tumour. The scientific term is to insert a "transgene" into CF33, which provides the soldier with instructions to generate and use the weapons.

VAXINIA / CF33-hNIS

VAXINIA is being used for the MAST clinical trial where CF33 is treating patients with metastatic solid tumours of various types. The hNIS ("human sodium iodide symporter") transgene provides instructions for displaying a flag on the tumour cell which attracts radioactive molecules such as its natural ligand iodine used in imaging of tumours. It provides the ability to see in real time where the CF33 virus is and therefore where the tumour is. This is an extremely powerful weapon not only to detect the tumour, but also converts CF33 into a synergistic radiotherapy drug.

CHECKvacc / CF33-hNIS-anti-PDL1

CHECKvacc also adds a precision weapon that, when released by the virus after infecting the tumour, releases the brakes on the localised immune response generated within the tumour microenvironment. This additional weapon, an immune checkpoint inhibitor, enables CHECKvacc to kill tumours systematically and comprehensively in multiple ways. Imugene is currently testing CHECKvacc in the very hard to treat triple negative breast cancer.

On-CAR-19 / onCARlytics / CF33-CD19

Imugene is developing a new weapon to eradicate tumours that has never been seen nor utilised in the fight against cancer. Still based on the same tumour targeting CF33, on-CAR-19 adds a weapon which creates a paradigm shift in the war against solid tumours. Cell therapies such as chimeric antigen receptor T-cell therapy (CAR T) have resulted in cures for the first time in liquid or blood tumours such as lymphoma. These liquid tumour weapons target a flag on the liquid tumour cells called CD19. This flag is specific for liquid tumours only and isn't found on solid tumours, which represent 90% of all tumour types. Until now, these modern weapons that have been so successful in curing liquid tumours, have been useless in the fight against solid tumours. Imugene's new CF33 platform

onCARlytics changes this. While CF33 is the same efficient tumour infecting and killing machine, adding the CD19 flag transgene to the CF33 soldiers' weaponry completely changes the fight against all cancer types by flagging the solid tumour cells with CD19 for eradication.

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.

About Eureka Therapeutics, Inc.

Eureka Therapeutics, Inc. is a privately held clinical-stage biotechnology company focused on developing novel T-cell therapies to treat cancers. Its core technology centers around its proprietary ARTEMIS® cell receptor platform and E-ALPHA® antibody discovery platform for the discovery and development of potentially safer and more effective T-cell therapies for the treatment of solid tumors and hematologic malignancies. The company currently has two clinical programs, ET140203 (ARYA1 for adults and ARYA2 for pediatrics) and ECT204 (ARYA3), in Phase I/II US trials in patients with advanced liver cancer.

Eureka Therapeutics, Inc. is headquartered in the San Francisco Bay Area. For more information on Eureka, please visit www.eurekatherapeutics.com. ARTEMIS® and E-ALPHA® are registered trademarks owned by Eureka.

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