



# IMUGENE

Developing Cancer Immunotherapies

Newsletter **May 2021**

**CF33 ADDS A NEW WEAPON, COMBINING WITH CAR T TO TREAT SOLID TUMOURS!**

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## CEO UPDATE

Hello and welcome, to the latest edition of our Imugene newsletter.

It is with true pleasure to bring you this latest update. I am proud to announce our recent acquisition of a remarkable new cancer treatment that we have designated, 'onCARlytics'.

### What is OnCARlytics?

OnCARlytics is a novel CD19 expressing oncolytic virus (CD19-CF33) from Dr Yuman Fong and Dr Saul Priceman's labs at the prestigious City of Hope Comprehensive Cancer Center in Los Angeles. Put simply, it's a solid tumour fighting combination treatment that puts together our oncolytic virus CF33, with CAR T cell therapy. A potent duality as you will discover by reading further.

### First, a bit of history

The latest step up from immunotherapy treatments (including our own CF33) is a cancer cellular therapy known as Chimeric Antigen Receptor Therapeutics (CAR T), and it has been found to be effective in treating blood cancers such as Acute Lymphoblastic Leukemia and non-Hodgkin Lymphoma. They express a protein signature called CD19. CAR T therapies that target CD19 have provided remarkable results in clinical evaluation of patients with blood cancers, achieving responses (reduction or no cancer) of around 60-90%. However, blood or liquid cancers only make up ~10% of cancers. So how do you target and treat the other ~90% of tumours (which are solid tumours) that CAR T cellular therapies don't target?

The scientists at City of Hope, pondered what would happen if you combine the known benefit of our cancer fighting immunotherapy product, CF33, to express CD19 on the tumour cell surface, then combine it with the CD19 targeting CAR T treatment? Now the CAR T's have something to target on solid tumours.

They quickly went from aspiration to activity. They started with our very own and unique oncolytic

virus, CF33, but with the insertion of a protein that expresses CD19 on its tumour cell surface. When combined with a CD19 directed CAR T therapy, it eradicated solid tumours in animals.

### Enter stage right our newest weapon in the Imugene arsenal... onCARlytics.

We now have a treatment that makes solid tumours visible to CD19 directed therapies like CAR T's, bispecifics and other therapeutics to target. Later in this bulletin we'll explain the mechanism of action, but for the moment, may I say that for CAR T therapies, solid tumour is the elusive Holy Grail and we hope that we are one step closer to seeing response levels that have been seen in liquid/blood cancers.

### I am also proud to share with you our milestones in our PD1-Vaxx and HER-Vaxx trials.

Firstly, we completed and cleared cohorts 1 and 2, and we are now at the highest cohort 3 dose of 100ug. This is our first in human study of PD1-Vaxx in patients with non-small cell lung (NSCLC), who have previously progressed on other treatments including other PD1 inhibitors.

Secondly, we have completed the enrolment of our Phase 2 HER-Vaxx trial. To date, it has shown very promising results, and we have now achieved our secondary end point of our protocol with 24 progression free survival events. We are delighted with the interim data results and doubly proud as they were published and presented at the prestigious American Association of Cancer Research conference held in April of this year.

### Please read on and discover how onCARlytics is going to truly make a positive difference in our ongoing efforts to defeat the scourge of cancer in all its forms.

With warmest regards,

**LESLIE CHONG**  
IMUGENE CEO

# ONCARLYTICS – THE TURNING POINT IN THE BATTLE TO DEFEAT SOLID TUMOURS

CAR T cell therapies are an exciting breakthrough in the treatment of cancer, particularly with blood cancers. Unfortunately, they represent only about 10% of all cancer types. The great and unmet need, is for treatments that attack the other 90% represented as solid tumours.

That's where we come in. To be the best tag team in cancer research is our game. Our oncolytic virus, onCARlytics (CF33-CD19), combined with CAR T cell therapy, is poised to change the face of cancer treatment. Each with their own set of attributes, the combination makes a formidable and effective weapon to tackle solid tumours.

OnCARlytics, invented by Dr Yuman Fong, Dr Saul Priceman, Dr Stephen Forman and Dr Anthony Park, is providing exciting initial data suggesting the combination of CAR T cell therapy plus onCARlytics, is more potent against solid tumours than CF33 therapy alone.

In pre-clinical trials that included testing triple-negative breast, pancreatic, prostate, ovarian, brain, head and neck cancer cell lines. This work was of such significance that it was recently featured on the front page of Science Translational Medicine.

Solid tumours are “immunologically cold,” meaning they are not typically responsive to immunotherapies that use the body's own immune system to fight cancer. Introducing our oncolytic virus, reversed the tumour's harsh microenvironment, making it more receptive to receiving CAR T cell treatment.

This combination therapy approach works by CF33-CD19 selectively infecting the solid cancer cells, replicating, and then the killed tumour cells release additional copies of the virus, propagating CD19 expression to adjacent tumour cells. Finally, the CD19-directed CAR T cells can recognise and attack these solid tumours.

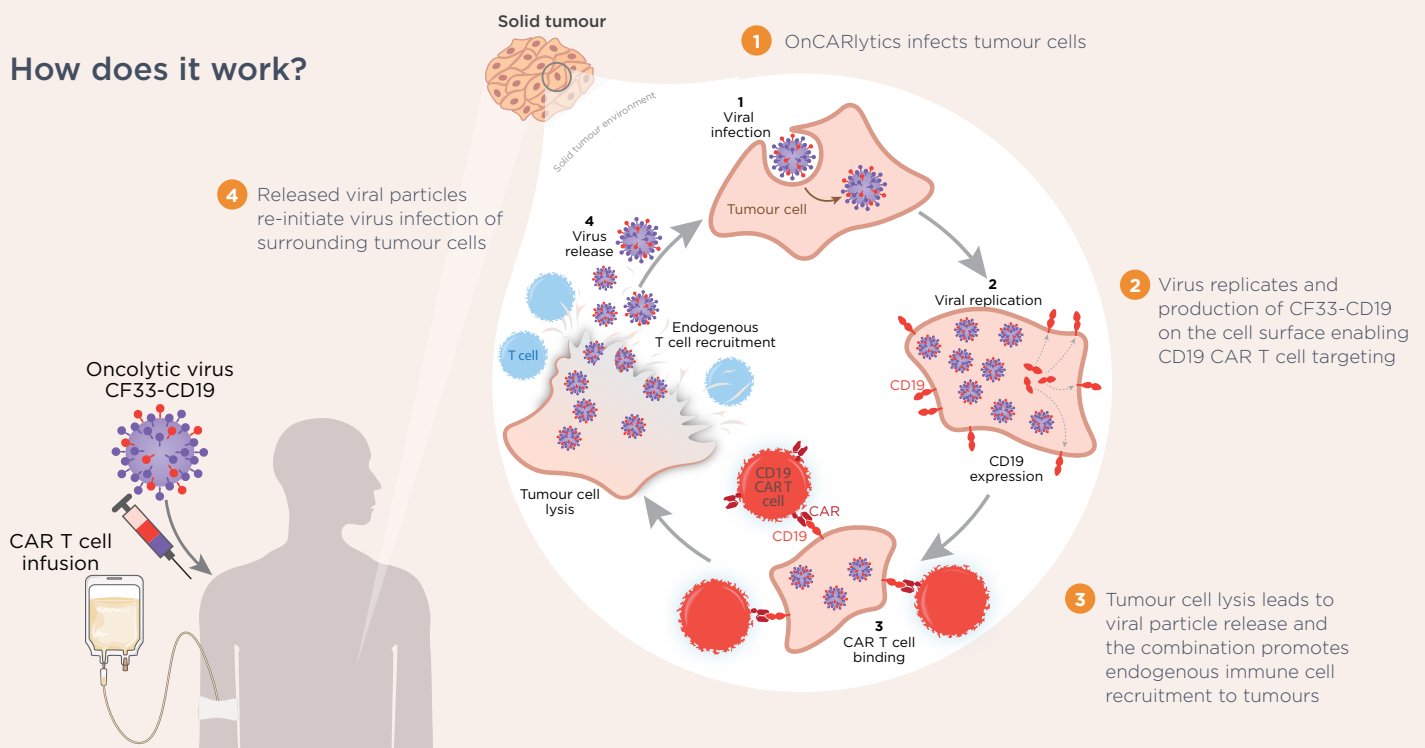
“The whole idea that you can turn a solid tumour into a quasi-B cell (liquid cancer) by introducing a CD19 antigen was clever and really novel,... The experiments were very well done, very convincing.”

**KATY REZVANI**

Transplant Immunologist at the MD Anderson Cancer Center



## How does it work?



## OnCARlytics the turning point in the battle to defeat solid tumours (cont).

### Chimeric Antigen Receptor Therapeutics (CAR T) cell therapy provides a ground-breaking innovative approach to strengthen the immune system in the fight against cancer.

Our body's immune system is made up of millions of cells that protect the body from infection and cancers. Importantly, this system includes T cells, which have the capacity to destroy abnormal cells within the body, including cancerous cells. However, when cancer cells invade the body, signals on their cell surface shield them from recognition by the immune system. Hence, the focus by the cancer research community on enhancing the immune system to recognise, attack, and destroy cancer cells.

To date, CAR T cell therapy has been shown to be effective in blood cancers only, including B cell Acute Lymphoblastic Leukaemia (in children) and Diffuse Large B cell Lymphoma (in adults).

CAR T cell therapy has demonstrated significant success and potential in such a short space of time, with KYMRIA<sup>®</sup>, YESCARTA<sup>®</sup>, TECARTUS<sup>®</sup>, and BREYANZI<sup>®</sup> securing FDA approvals. Blood cancer diagnoses, once thought of as terminal with no other options to explore, are now providing durable and meaningful remissions for patients. The potential is huge, and only beginning to be untapped.

We have the ability to combine onCARlytics with other CAR T in development, including off-the-shelf, bispecifics, ADCs and essentially any treatment against CD19.

#### The process of CAR T cell therapy is complex, and includes:

- Collecting a sample of the patient's own T cells via a blood draw
- Re-engineering the T cells in clinical laboratory conditions to carry structures known as Chimeric Antigen Receptors (CARs) on their surface – these are engineered molecules, that don't exist in the human body
- Reinjecting the turbo-charged T cells back into the patient
- Allowing the T cells to rapidly multiply and engineer their receptors to identify, attack and destroy cancer cells throughout the body which present the engineered receptor on their surface.



# THE BIRTH OF ONCARLYTICS

Our scientists at The City of Hope took a collaborative approach to finding a better immunotherapy cancer treatments. A few years ago, Priceman, Fong and Stephen J. Forman, M.D., leader of City of Hope's Hematologic Malignancies Research Institute, met to brainstorm how they might combine their expertise, namely oncolytic virus and CAR T cell therapies, to target solid tumours.

The trial will first test the safety of CF33-CD19 in patients with solid tumours. If that is found to be safe and effective, the oncolytic virus and CAR T cell therapy will then be tested in sequence. The trial is anticipated to start in 2022.

A picture being worth a thousand words, have a look at the video interview a with Dr Priceman and his colleague, Dr. Park at [youtube.com/watch?v=hRd15I\\_H\\_xA](https://www.youtube.com/watch?v=hRd15I_H_xA). They sum up in clear language what they have achieved and subsequently where we are going with this remarkable new technology.

“It was a simple concept but one that took many steps to get us to where we are today in teaming up with Imugene – we are now designing a clinical trial to test this combination in patients”

DR PRICEMAN



# PERSPECTIVES FROM THE INVENTORS

## DR YUMAN FONG

Sangiaco Chair and  
Chairman, Department of  
Surgery, City of Hope Medical  
Centre and Chair of Imugene's  
Oncolytic Virotherapy Scientific  
Advisory Board.



### Dr Yuman Fong on the potential and anticipation of OV's and CAR T cell therapy

An Oncolytic Virus (OV) is a virus that specifically infects and kills cancer cells while leaving normal cells uninfected and healthy. In cancer, OV's work in a number of ways:

- Firstly, by directly killing the cancer cells
- Secondly, by attracting the patient's immune cells to target and kill the cancer cells; and
- Thirdly, by "turning on" cancer cell proteins so they become targets for highly effective therapies like CAR T cell therapy.

According to Dr Fong, OV's like CF33, hold the promise of being able to 'hunt down' widely metastasised cancers, and eradicate them using the patient's own immune function, together with highly effective immunotherapies like CAR T cell therapy. What makes CF33 unique, is its ability to hold the gene for the CD19 protein. This allows the CF33 OV, to identify and target cancer cells throughout the body, and force the expression of CD19 on the cell surface, so that CAR T cell therapy can then attack and destroy the cancer cells.

For Dr Fong, CF33-CD19 in combination with CAR T cell therapy would revolutionise the way we treat cancers. "Theoretically our CF33-CD19 can target any cancer including brain, breast, ovarian, lung and colon cancers for eradication by clinically available CAR T therapy. This makes many common solid tumour cancers targetable both by an OV and by CAR T, two of the most highly anticipated and promising immunotherapies for the treatment of cancer."

## DR SAUL PRICEMAN

Assistant Professor,  
Department of Hematology  
and Hematopoietic Cell  
Transplantation, City of Hope  
Medical Centre.



### Dr Saul Priceman on the paradigm shift in the way we treat cancer

Targeting cancer cells with immune cells has been the holy grail of cancer therapy. It has the potential to potently and durably eradicate cancer cells, and spark an immune response that allows the same T cells, plus the patient's own immune system, to continue to target their cancer as a living and evolving drug.

According to Dr Priceman, the way CF33-CD19 works with CAR T therapy is simple. "We reasoned that if OV's like CF33 can infect tumour cells and deliver genes of interest to potentiate an anti-cancer response, why couldn't they also deliver a gene (CD19), which could then redirect the most effective CAR T cell therapy to target solid tumours? It is this combination approach, that allows for universal therapy with the potential to target any solid tumour."

This true synergy between CF33-CD19 and CAR T therapy is the first of its kind, in effectively targeting solid tumours, according to Dr Priceman. "The idea that an OV can turn any solid tumour into one that can be targeted with a CD19 CAR T, opens up tremendous opportunities to expand the utility of OV's in general, and in applying CAR T cell therapy to more than just blood cancers."

"We believe we can now extend the remarkable successes of CD19 CAR T cell therapy into patients with ovarian, pancreatic and colorectal cancers to name only a few. This represents a paradigm shift in the way we treat cancer. With CF33-CD19, we believe we can turn any intractable tumour type into one that can be potently targeted and eradicated by the combination of CF33-CD19 and CAR T cell therapy".



## FROM THE CHAIR

**Hello again, and may I extend the hope that you are still coping with the influence of COVID-19, be it at home or at the office. I look to the day that it becomes a memory we will not revisit.**

As your Executive Chairman, I am privileged to be involved with the development of your company and the remarkable efforts of our Managing Director and CEO, Leslie Chong and her team.

Every once in a while, events unfold that are not part of what you originally expected. This is one of those times. We, as you will read about in this bulletin, have taken on a task that has to date been unanswered in the field of cancer research.

We are targeting, and are on the path to finding, a way to fight cancer at the tumour level. It is, as our illustrious colleague at City of Hope Dr Saul Priceman puts, it "the holy grail of cancer research".

It's all about duality of effort. In our corner we have our cancer fighting oncolytic virus CF33, and waiting in the wings are the equally ferocious ingredients making up what is known as CAR T cell therapies.

Whilst we will remain an immuno-oncology company, the opportunity to work with partners in cell therapy and in particular CAR Ts, is very exciting.

Put them together, and we have the chance to make medical history. We have expanded upon how we intend to achieve this.

Our relationship with the City of Hope is blossoming indeed. Here in Australia, we are backing their efforts with our own business focus to bring this new technology to the attention of sophisticated investors throughout the country.

Our website has full details on this new and innovative technology and as always, Leslie and I are available should you have any questions outside the normal flow of information from us.

With kind regards,

**PAUL HOPPER**

## HIGHLIGHTS

### WORLDWIDE EXCLUSIVE

license to novel technology which provides Imugene's CF33 oncolytic virus the ability to utilise CD19 CAR T

### THERAPIES AGAINST SOLID TUMOURS

### COMPELLING PRE-CLINICAL

### ACTIVITY

in TNBC, colorectal, pancreatic, prostate, ovarian, head and neck and glioma cancers when combining onCARlytics (CF33-CD19) with CD19 CAR T

### THE FOUR FDA APPROVED

CD19 CAR T drugs only work in blood cancers...

### SOLID TUMOURS REMAIN THE HOLY GRAIL

this technology makes the treatment of solid tumours by CAR T DRUGS VIABLE

### PHASE 1 CF33 ONCOLYTIC VIRUS STUDIES

commencing shortly, will accelerate development of the onCARlytics

### OFFERS IMUGENE NUMEROUS PARTNERING OR COLLABORATION OPPORTUNITIES

for both approved and in-development CAR Ts onCARlytics makes the treatment of solid tumours by CAR T drugs viable

## 4yr



### SPONSORED

RESEARCH AGREEMENT with City of Hope Cancer Centre to further develop the technology

OnCARlytics Phase 1 study to commence in 2022

Robust intellectual property with long patent life

Enhancement of our scientific team to spearhead clinical development of onCARlytics

Attractive industry standard licensing terms and royalty rates





**IMUGENE**  
Developing Cancer Immunotherapies

ASX: IMU

⋮ About

⋮ Imugene is a clinical stage  
⋮ immuno-oncology company  
⋮ developing a range of new  
⋮ treatments that seek to  
⋮ activate the immune system  
⋮ of cancer patients to identify  
⋮ and eradicate tumours.  
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