IMUGENE
Developing Cancer Immunotherapies

ASX: IMU

Imugene Licenses CD19 Oncolytic Virus to Turn CAR T Therapy Against Solid Tumours

18th May 2021

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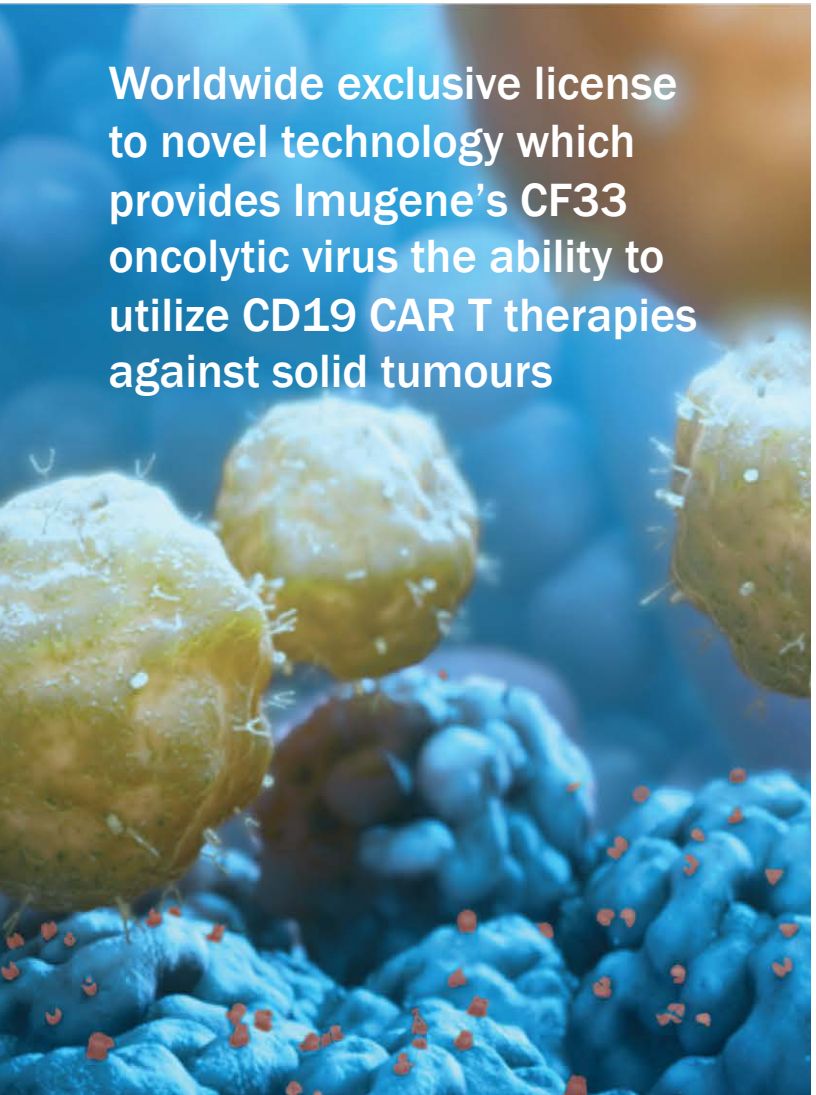
Investment Highlights



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

Offers Imugene numerous partnering or collaboration opportunities for both approved and in-development CAR Ts, bispecifics, ADC's etc

Enhancement of our scientific team to spearhead clinical development of onCARIytics

Compelling pre-clinical activity

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

Phase 1 CF33 oncolytic virus studies, commencing shortly will accelerate development of onCARIytics

Attractive industry standard licensing terms and royalty rates

OnCARIytics Phase 1 study to commence in 2022

Robust intellectual property with long patent life

Four-year Sponsored Research Agreement with City of Hope Cancer Centre to further develop the technology

Introducing onCARIytics

"OnCARIytics makes the treatment of solid tumours by CAR T drugs viable"

Dr Saul Priceman

OnCARIytics is a novel and effective combination immunotherapy utilizing its exclusively licensed CF33 oncolytic virus to deliver and present cell surface CD19 antigen (CF33-CD19) promoting CD19 CAR T cell anti-tumour responses against solid tumours

Watch:
Combination CAR T Oncolytic Virus Immunotherapy Kills Tumours

Dr's Saul Priceman and Anthony Park from the City of Hope Cancer Centre

The CAR T Solid Tumour Challenge & Imugene's Solution

Chimeric Antigen Receptor (CAR) T cell therapy has had limited activity in solid tumours, largely due to a lack of selectively and highly expressed surface antigens, such as the blood B cell antigen CD19.

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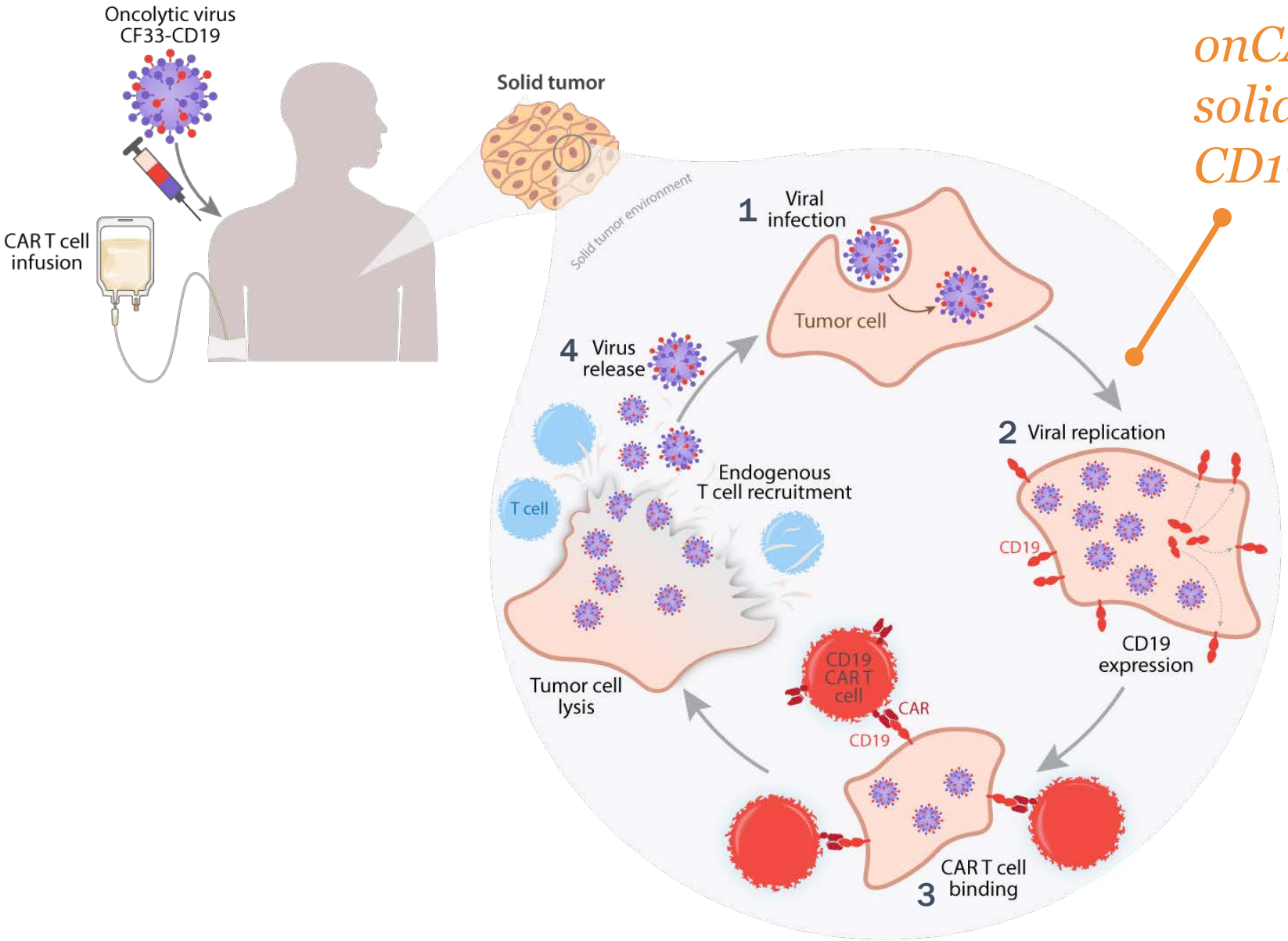
NEW CONCEPT

Utilise OV's as a delivery vector to deliver CD19 antigen to solid tumour cells

Engineer Imugene's CF33 to infect solid tumour cells and insert CD19 transgene to enable presentation of CD19 over the tumour cells during tumour cell infection, onCARlytics (CF33-CD19)

Combination use of autologous or allogeneic CD19 CAR Ts (eg. Novartis KYMRIAH®) with onCARlytics (CF33-CD19) presents CD19 targets on solid tumours

Mechanism of Action: How does it work?



onCARlytics makes solid tumours "seen" by CD19 directed CAR T

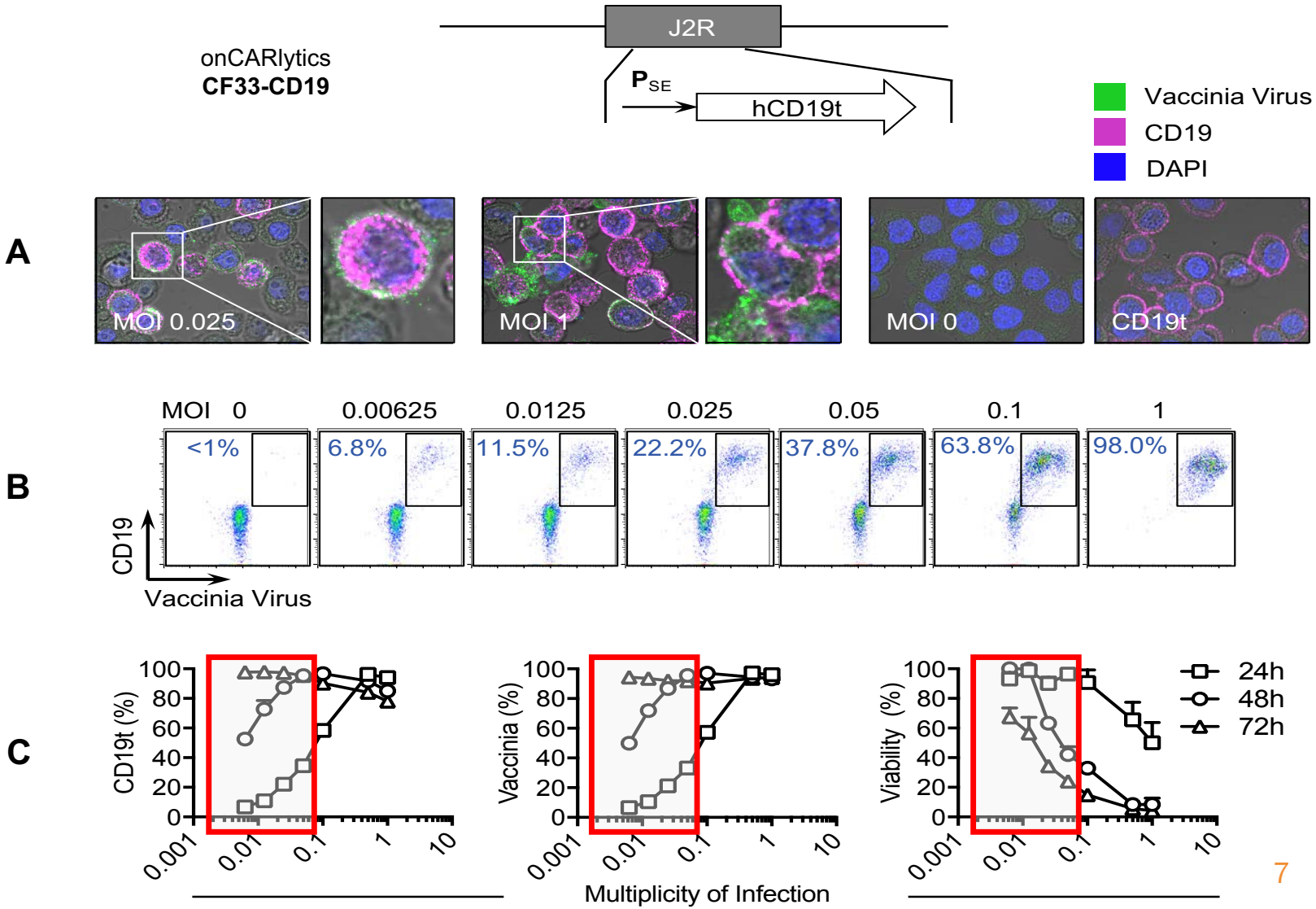
1. OnCARlytics infects tumour cells
2. Virus replication and production of CF33-CD19 on the cell surface enabling CD19 CAR T cell targeting
3. Tumour cell lysis leads to viral particle release and the combination promotes endogenous immune cell recruitment to tumours
4. Released viral particles re-initiate virus infection of surrounding tumour cells.

onCARIytics Delivers CAR Targets to "*Targetless*" Solid Tumours

A. Immunofluorescence microscopy of MDA-MB-468 cells infected for 24 hours with CF33-CD19 at multiplicity of infection (MOI) of 0.025 or 1, untransduced (MOI of 0), or cells transduced with lentivirus to stably express CD19t. Blue is DAPI, pink indicates CD19t, and green indicates vaccinia.

B. Fluorescence-activated cell sorting (FACS) plots of MDA-MB-468 tumour cells positive for CD19t and vaccinia virus after 24 hours of CF33-CD19 infection at increasing MOIs. Percent indicates CD19t+, virus-positive population in the boxed region.

C. Quantification of percent CD19t+ (left), vaccinia+ (middle), and viable (right) MDA-MB-468 tumour cells after 24-, 48-, and 72-hour exposure to the indicated MOIs of CF33-CD19.

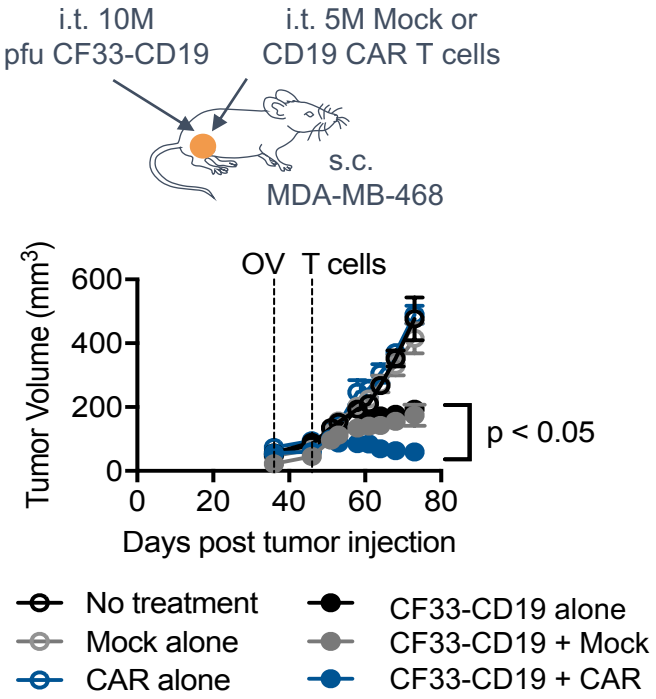


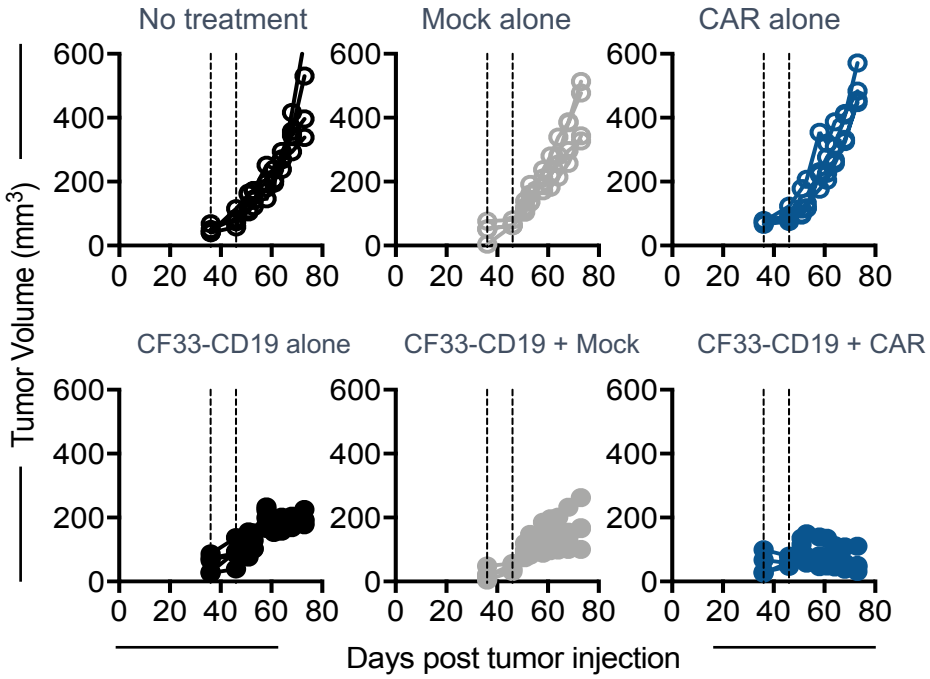
Park AK, Fong Y, Kim SI, Yang J, Murad JP, Lu J, Jeang B, Chang WC, Chen NG, Thomas SH, Forman SJ, Priceman SJ.Sci Transl Med. 2020 Sep 2;12(559): eaaz1863. doi: 10.1126/scitranslmed.aaz1863.PMID: 32878978

onCARIytics Drives CD19 CAR T cell Anti-Tumour Responses in Solid Tumours

Antitumour efficacy of combination therapy of CF33-CD19 and CD19 CAR T cells in human xenograft tumour models.

MDA-MB-468 tumour–bearing mice treated with CF33-CD19 and CD19 CAR T cells. NSG mice were injected subcutaneously with MDA-MB-468 (5 × 106 cells) on day 0, and tumours were injected with CF33-CD19 (107 pfu, 10 M) on day 36. On day 46, tumours were injected with either untransduced T cells (mock) or CD19-CAR T cells (CAR; 5 × 106 cells).





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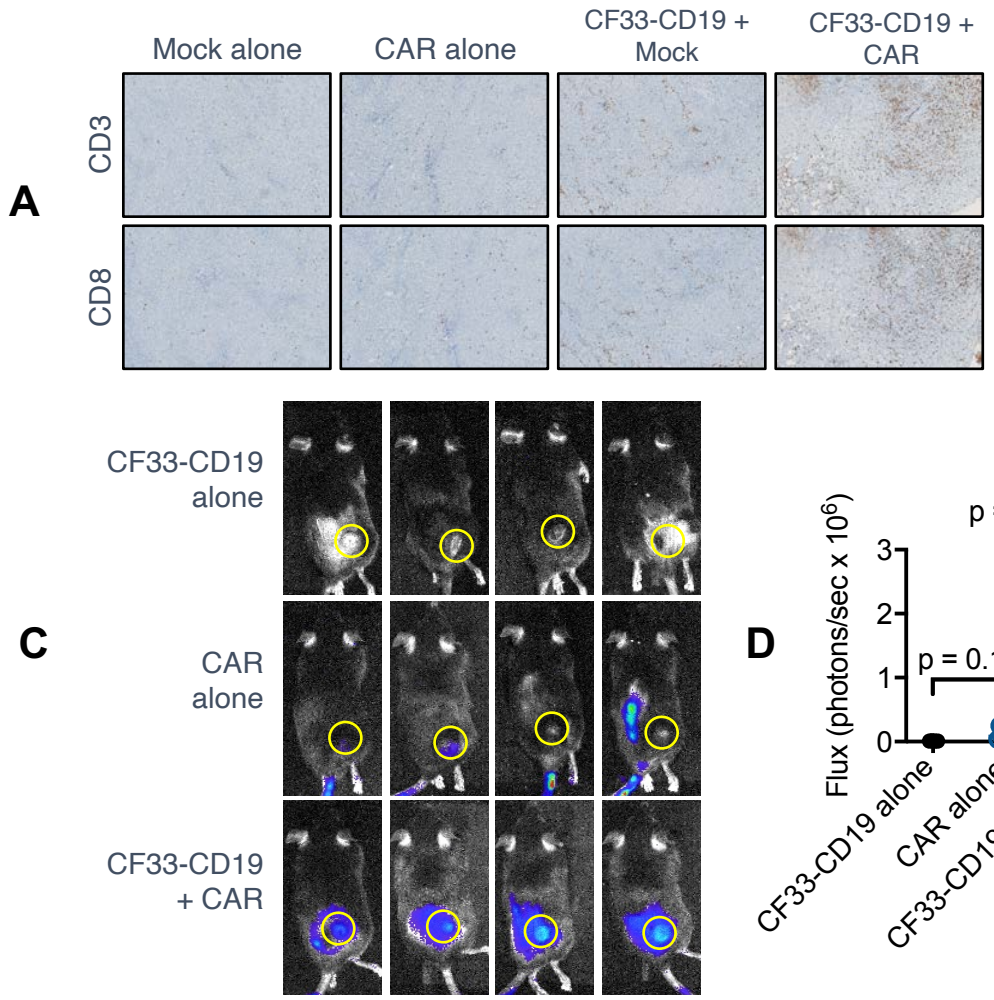
Combination of CF33-CD19 and CD19 CAR T cells promotes tumour regression in xenograft model of TNBC

onCARlytics promotes endogenous & CAR T cell tumour infiltration



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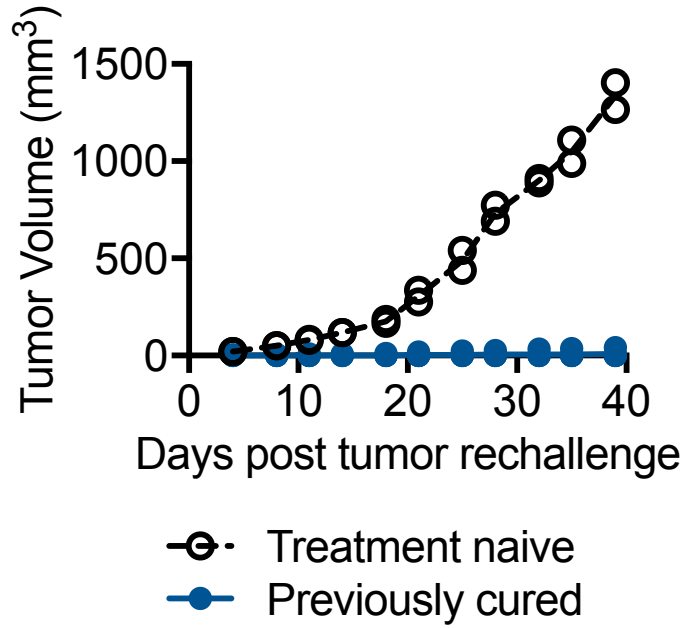
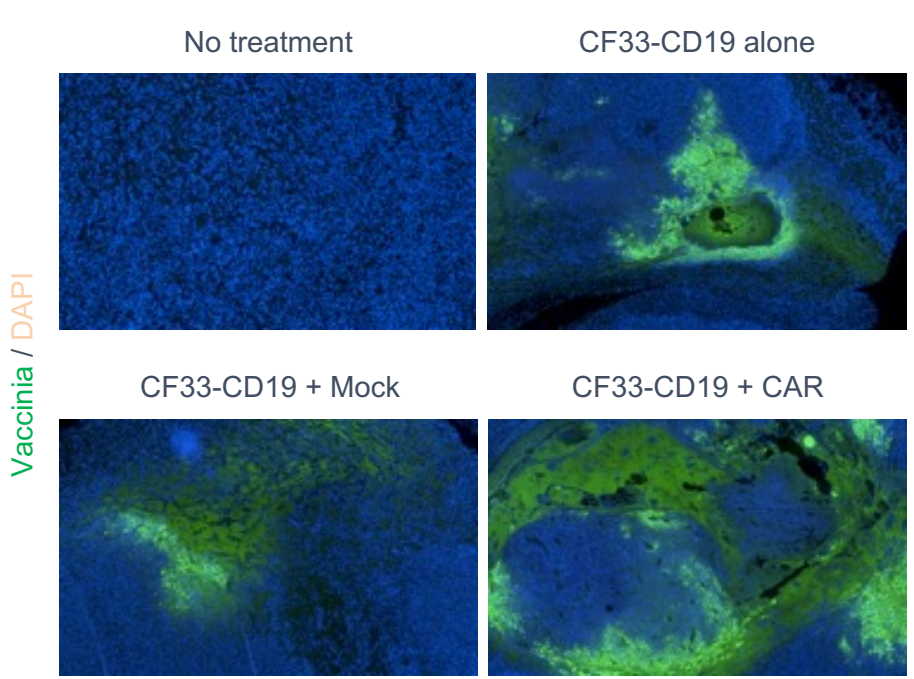
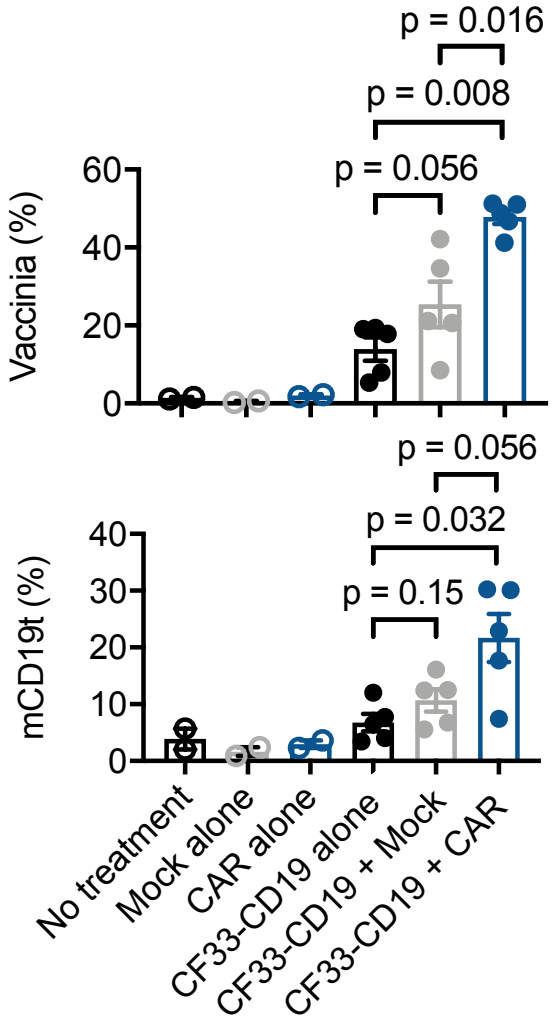
Combination of CF33-CD19 and CD19 CAR T cells promotes endogenous cytotoxic T cells, CAR T cells & memory T cell responses



A. Histology showing murine CD3+ and CD8+ T cells in subcutaneous MC38 tumours harvested from mice treated intravenously with untransduced T cells (mock) alone, mCD19 CAR T cells alone, CF33-CD19 + mock T cells, and CF33-CD19 + mCD19 CAR T cells. Tumours were harvested 4 days after T cell administration and 6 days after CF33-CD19 injection.
B. Quantification of immunohistochemical staining for murine CD8+ cells in tumours from mice treated as in (A). Symbols indicate individual tumours from mice.
C. Representative flux imaging of mice 2 days after treatment with intratumoural CF33-CD19 alone (n = 4), intravenous firefly luciferase–expressing mCD19 CAR T cells alone (n = 5), or CF33-CD19 + firefly luciferase–expressing mCD19 CAR T cells (n = 10).
D. Quantification of T cell flux from the regions of interest shown in (C).
E. Tumour volume in treatment-naïve or previously cured C57BL/6j mice rechallenged by subcutaneous injection of MC38 (5 × 105) cells. n = 7 for rechallenge group, n = 2 for treatment-naïve group. Individual tumours from mice are shown.

CD19 CAR T with onCARlytics Amplifies Intratumoural Virus Spread *In Vivo*





A. Histology showing vaccinia virus in MC38 tumors harvested from mice with no treatment or treatment with CF33-CD19 alone, CF33-CD19 + mock T cells, and CF33-CD19+ mCD19-CAR T cells. T cell treatment was 2 days after CF33-CD19 injection. Tumors were harvested and stained for vaccinia virus (green) 4 days after CF33-CD19 alone or 2 days after T cell treatments.

B. Quantification of percent cells positive for vaccinia and mCD19t in subcutaneous tumors from mice receiving the indicated treatments. Mice were injected subcutaneously MC38 tumors (5 × 105 cells) on day 0. On days 14 and 16, mice were intratumorally injected with OVm19t (5 × 107 pfu per mouse). On day 18, mice were treated intravenously with mock T cells or mCD19-CAR T cells. Tumors were harvested 5 days after CF33-CD19 or 3 days after T cell treatments. Cells were analyzed by flow cytometry. n = 2 to 5 per group

Combining CD19 CAR T with CF33-CD19 supercharges viral spread in solid tumours

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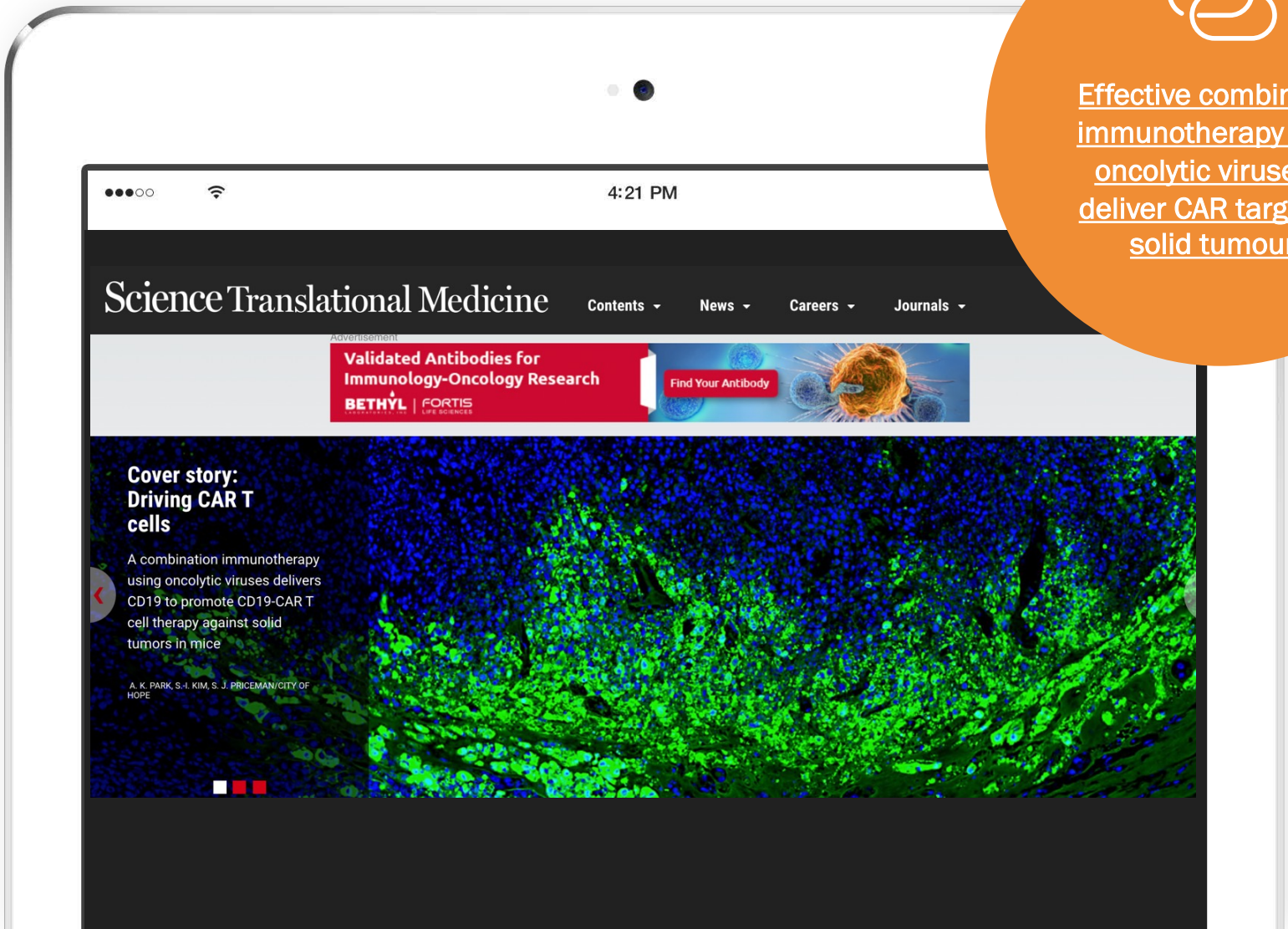
Published Front Cover of Science Translational Medicine Journal in 2020



Effective combination immunotherapy using oncolytic viruses to deliver CAR targets to solid tumours

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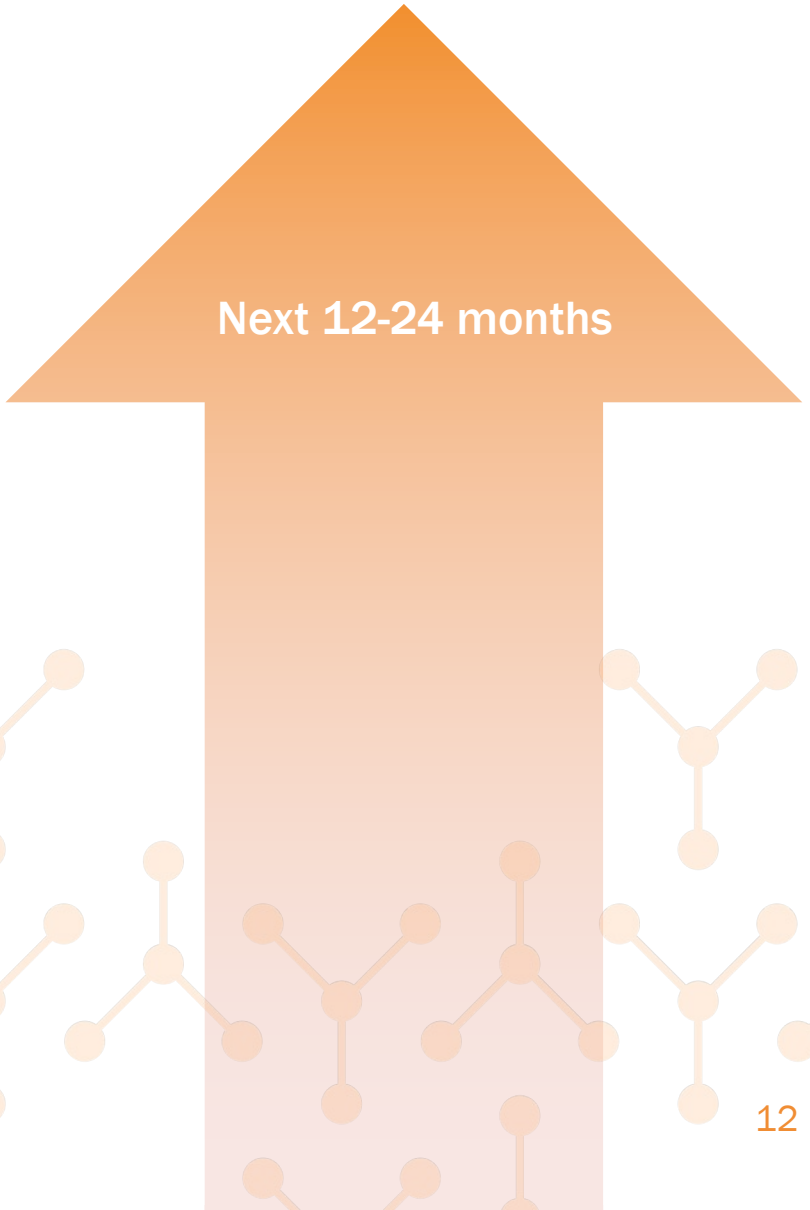
Milestones



- GMP manufacturing for pre-clinical toxicology & Phase 1 study
- FDA Pre-IND Meeting
- GLP Toxicology Study
- FDA IND Clearance
- 1st Patient Dosed Monotherapy
- 1st Patient Dosed Combination Therapy
- Recommended Phase 2 Dose Established & Expansion Opened

Four FDA Approved CD19 CAR T's

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Approved and in-development autologous or allogeneic CD19 CAR Ts can be partnered with Imugene's onCARlylics for treating solid tumours:

KYMRIAH® (tisagenlecleucel) Suspension for IV infusion
NOVARTIS

YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion
GILEAD

TECARTUS™ (brexucabtagene autoleucel) Suspension for IV infusion
Kite

Breyanzi® (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION
Bristol-Myers Squibb

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Intellectual Property

FOUNDATION PATENT (2038)

PCT	US2019/033030
Title	Oncolytic virus expressing a CAR T cell target and uses thereof
Inventors	Fong, Priceman, Forman, Chen & Park
Assignee	City of Hope
Primary Date	11 August 2017
International Publication	14 February 2019
Expiration Date	2038

PCT application filing date was 10/8/2018 and estimated expiration date is in **late 2038**. The patent application includes both composition of matter and method of use. It is currently pending with the opportunity to secure worldwide rights. International search report was favorable for composition of matter.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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C07K 14/705 (2006.01) *C12N 7/02* (2006.01)
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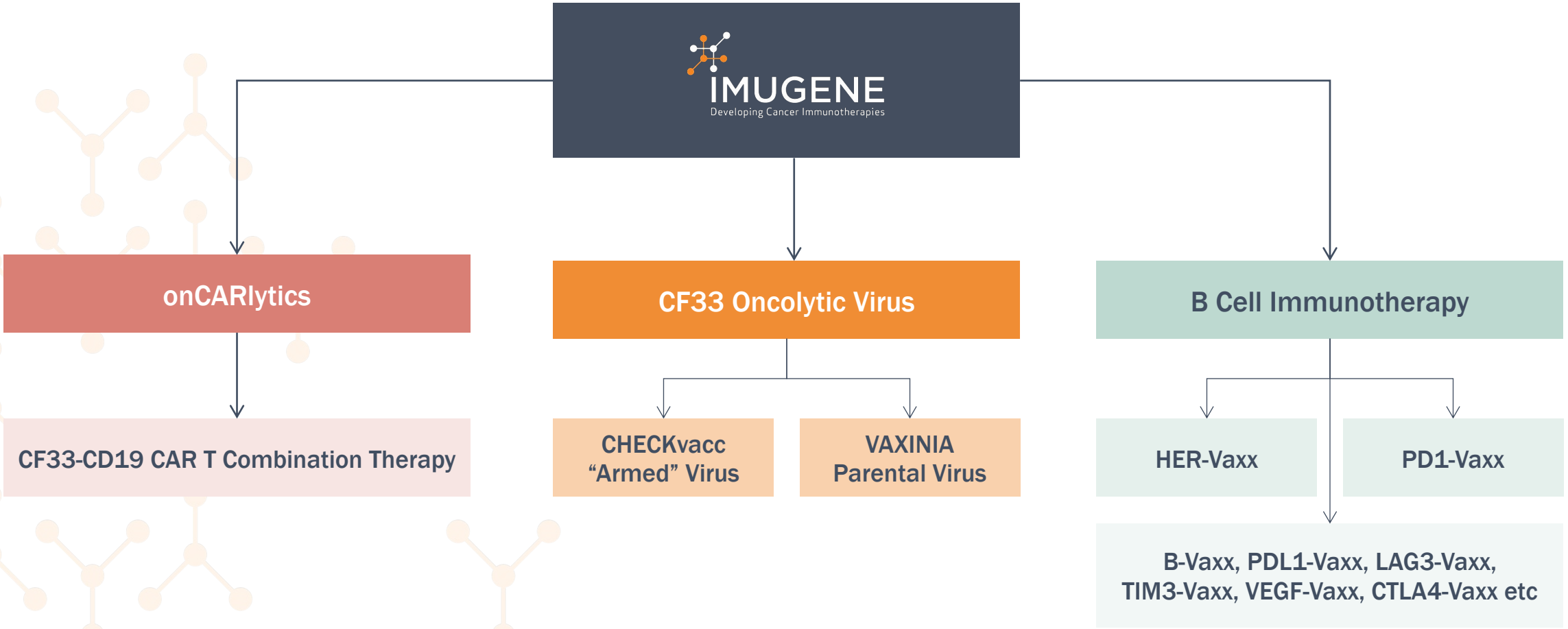
Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

Three Novel Technology Platforms



Summary and Projections

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

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