IMUGENE
Developing Cancer Immunotherapies

ASX: IMU

IMUGENE

October, 2021

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Introduction to Imugene

Imugene is a biotech company headquartered in Australia and publicly traded on the Australian Securities Exchange (ASX:IMU)

2013

Paul Hopper built Imugene around a technology that originated from the Medical University of Vienna

2015

Leslie Chong from Genentech joined Imugene

2017

HER-Vaxx, our HER-2 targeted B Cell Immunotherapy entered the clinic

2018

Licensed extensive B cell portfolio and platform from OSU and Mayo Clinic comprising of PD1, HER1, HER2, HER3, VEGF, IGF-1R, CD28

2019

Completed the acquisition of a prolific oncolytic virus from City of Hope invented by Dr Yuman Fong

MAY 2021

Licensed onCARIytics from City of Hope invented by Dr Y Fong, Dr S Priceman & Dr A Park

SEP 2021

Entered the S&P/ASX 300 Index

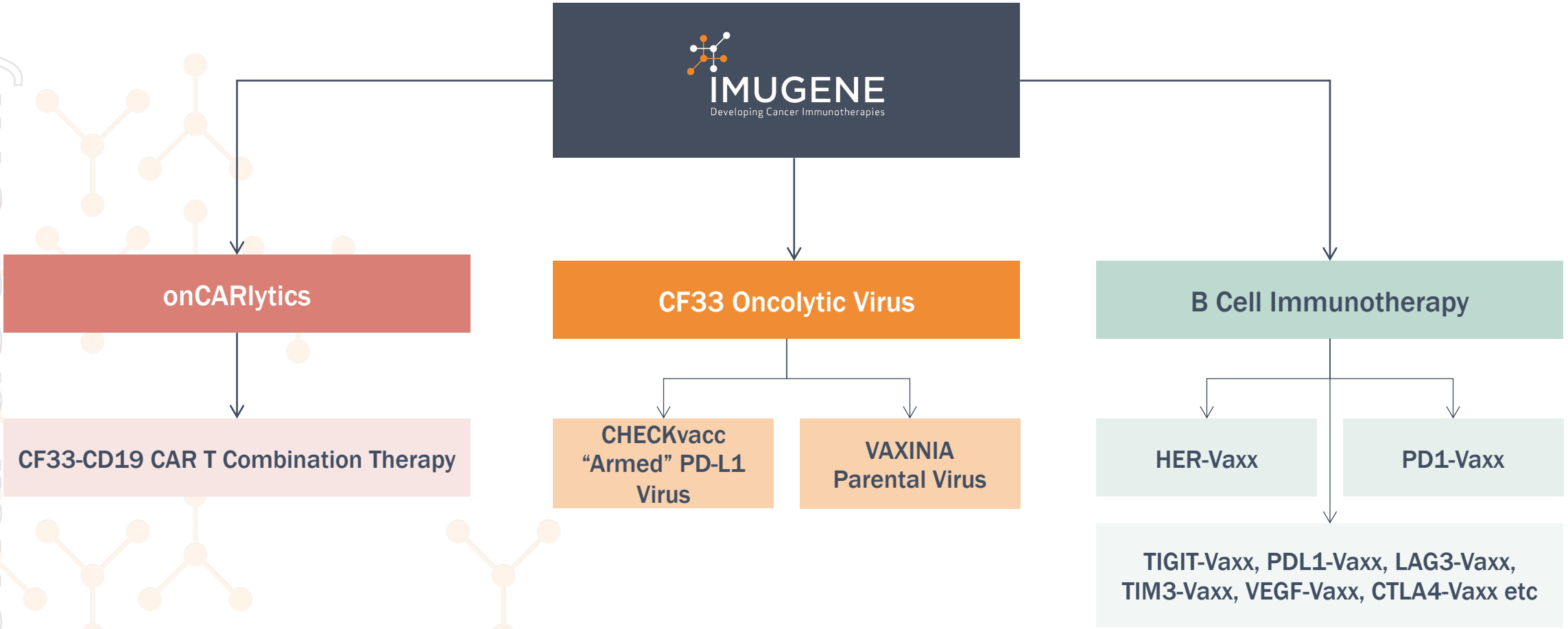
AUG 2021

Strategic Partnership with Celularity

Investment Highlights

- Three novel technology platforms: Oncolytic virotherapies, onCARIytics in cellular therapy and B-Cell activating immunotherapies
- B-Cell Technologies: HER-Vaxx Phase 2 in gastric cancer and PD1-Vaxx in NSCLC
- CF33 Oncolytic Virotherapies: 2 (CHECKvacc and Vaxinia) Phase 1 Clinical Trials
- OnCARIytics: Pre-clinical Toxicology Trials and strategic partnership with Celularity
- Highly experienced team in oncolytic virus and cellular therapies
- Significant news flow with multiple near & medium term valuation inflections

Three Novel Technology Platforms



Imugene's Deep Pipeline

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Technology	Program	CMC & Pre-Clinical	IND	Phase I	Phase II	Key Data / Results	Intellectual Property
onCARlytics	**CF33-CD19**					• Compelling pre-clinical activity in multiple cancers when combining onCARlytics (CF33-CD19) with CD19 CAR T • Combination of onCARlytics and CD19 CAR T cells promotes endogenous memory T cell responses • Research agreement with Celularity's s allogeneic CAR T (CyCART-19)	**Expiring 2038**
VAXINIA (CF33-hNIS)	**MAST** (Solid tumours)					• CF33 has shown strong anti tumour responses in preclinical studies • Inhibition of tumour growth in nearly all NCI60 models in TNBC, Lung, Pancreatic etc. • Signs of increased tumour growth inhibition with CF33 + anti PD-L1	**Expiring 2037**
CHECKvacc (CF33-hNIS-aPD-L1)	**COH TNBC IST** (Breast Cancer)					• Potentially solves the industry problem of additive toxicity of combined checkpoint inhibitors if safety of CF33 is maintained in combination • FDA IND approval, Phase 1 IST Open	**Expiring 2037**
HER-Vaxx (HER-2)	**HERIZON** (First line Gastric Cancer)					• Two further company sponsored Phase 2 studies and one Investigator Sponsored Study with HER-Vaxx in early and late stage gastric cancer are in planning • Phase 2 Interim data: 0.418 HR (80% 2-sided CI: 0.186, 0.942); 14.2 months HER-Vaxx + chemo compared to 8.8 months chemo alone • Strong phase 1b results with no safety or toxicity issues, all patients had increased antibody response, 11/14 evaluable patients with encouraging clinical responses	**Expiring 2036**
	neoHERIZON (Neoadjuvant Gastric Cancer)						
	NextHERIZON (Metastatic Gastric Cancer)						
PD1-Vaxx (PD-1)	**IMPRINTER** (Lung Cancer)					• PD1-Vaxx has shown encouraging response in preclinical studies • Strong inhibition of tumour growth in mouse models of colorectal cancer (outperformed industry standard mouse PD-1 mAb) • Signs of increased tumour growth inhibition when co-administered with B-Vaxx • FDA IND approval, First patient dosed December 2020	**Expiring 2037**

International Leadership Team with Extensive Commercialisation Expertise in the Sector

Imugene has a team with oncology drug development experience

Leslie Chong

SYDNEY, AU

Managing Director & CEO

- 23+ years of oncology experience across Phase I – III clinical development programs
- Ex Senior Clinical Program Lead at Genentech, one of the world's most successful biotech businesses which sold the best selling breast cancer drug Herceptin
- Also worked at global majors GSK and Exelixis
- Non-Executive Director of Cure Brain Cancer Foundation (CBCF) & Chimeric Therapeutics

Paul Hopper

SYDNEY, AU

Executive Chairman

- Founder and Chairman of Imugene
- Founder & Chairman of Chimeric Therapeutics
- Chairman of SUDA Pharmaceutical
- Former Chairman of Viralytics
- Founder & Director of Prescient
- Extensive international & ASX biotech capital markets experience particularly in immuno-oncology & vaccines

Dr Jens Eckstein

CAMBRIDGE, USA

Non-Executive Director

- Managing Partner of Apollo Ventures
- Former president of SR One Ltd., the VC arm of GSK
- 15+ years in VC experience funding early to clinical stage biopharmaceutical companies
- Extensive experience as chairman, board director and founder of several biotechnology and venture capital companies.
- Creator of OneStart, the world's largest life science accelerator

Dr Lesley Russell

PHILADELPHIA, USA

Non-Executive Director

- 25+ years of senior international operational and leadership experience having worked at Amgen, Eli Lilly, Teva, and Cephalon
- Extensive knowledge and experience with new drug development
- Non-Executive Director of Enanta Pharmaceuticals.

Dr Axel Hoos

PHILADELPHIA, USA

Non-Executive Director

- CEO of Scorpion Therapeutics
- Former Senior Vice President and Head of Oncology at GSK
- Former Medical Lead for Yervoy, the first immuno-oncology treatment to improve first survival .
- Board of Director of TCR^2 Therapeutics in Boston
- Chairman of the Sabin Vaccine Institute
- Co-Chair of the Cancer Immunotherapy Consortium Think-Tank

Charles Walker

BRISBANE, AU

Non-Executive Director

- Experienced listed biotech CEO and CFO (ASX:ACL and ASX:IMU)
- Extensive financial markets experience having executed 50+ cross border transactions
- Clinical experience includes managing pipeline of drugs in all stages from discovery, through to Phase III to product launch
- CEO, Founder and NED of RedEarth Energy Storage

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B-Cell Immunotherapies

B Cell Based Antibodies Have Distinct Advantages To Existing Treatments

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B cell Vaccines offer a unique opportunity to intervene at multiple points in the immune system and create immune memory which enhances durability of response.

NATURAL B CELL DERIVED ANTIBODIES

MONOCLONAL ANTIBODIES

Safety	Stimulates the immune system to produce Abs, which may be potentially safer	Synthetic Ab, with side effects (including ventricular dysfunction, CHF, anaphylaxis, immune mediation)
Efficacy	Polyclonal Ab response reduces risk of resistance and potentially increases efficacy	Monoclonal Ab – may develop anti-drug antibodies
Durability	Antibodies continuously produced with lasting immune response to potentially inhibit tumor recurrence	Half life necessitates recurrent dosing
Usability	Potentially low numbers of vaccinations required per year	Requires regular infusion
Cost	Low cost of production enables greater pricing flexibility facilitating combination	Expensive course of treatment >US$100K per year

HER-Vaxx Phase 2 Recruitment Complete

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Trial
- Phase 2
- Open label
- Asia
- Eastern Europe
- India

Patients
- HER-2+++
- HER-2++ FISH/CISH +ve
- Advance or metastatic Gastric Cancer
- Stage IIIb/IV
- 36 patients in two arms

Study

Randomised

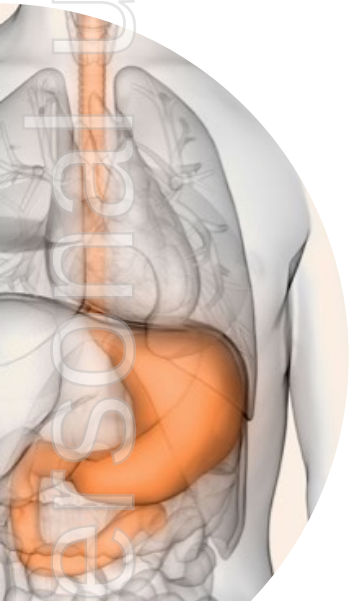
HER-Vaxx in combination with standard of care chemotherapy

Or

Standard of care chemo: Cisplatin and 5FU or capecitabine or oxaliplatin

Primary Endpoints
- Overall survival

Secondary Endpoints
- Progression-free survival
- Safety and Tolerability
- Immune response



First patient dosed March 2019/Last patient enrolled Jan 2021

Days	-21	0	14	21	35	42	63	77	84	105	126 +42	140 +63
IMU-131 administration		✓	✓		✓			✓				✓
Chemotherapy Cycle		1		2		3	4		5	6		

Max 6 cycles SOC chemo with progression assessment every 42 days

AACR 2021 Presentation Poster

Abstract No. CT107

A PHASE 1B/2 OPEN-LABEL STUDY WITH RANDOMIZATION IN PHASE 2 OF IMU-131 HER2/NEU PEPTIDE VACCINE PLUS STANDARD OF CARE CHEMOTHERAPY IN PATIENTS WITH HER2/NEU OVEREXPRESSING METASTATIC OR ADVANCED ADENOCARCINOMA OF THE STOMACH OR GASTROESOPHAGEAL JUNCTION

Interim Analysis Results

Marina Maglakelidze[1], Dinara Ryspayenva[2], Iurie Bulat[3], Zoran Andric[4], Ivan Nikolic[5], Tanuj Chawla[6], Rajnish Nagarkar[7], Vaibhav Choudhary[8], Giri Venkata[9], Rajesh Kumar Singh[10], Davorin Radosavljevic[11], Zoran Petrovic[12], Ursula Wiedermann[13], Leslie Chong[14], Rita Laeufle[14] Nicholas Ede[14], Bonnie Nixon[14], Anthony Good[14]

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INTRODUCTION

HER-Vaxx (**IMU-131**) is a **B-cell activating immunotherapy** consisting of three fused B-cell epitopes (p467) from the HER2/neu extracellular domain coupled to CRM197 and administered with the adjuvant Montanide.

The Phase 2 part of the study hypothesizes that active immunization with HER-Vaxx (IMU-131) will replicate or improve efficacy and safety of the approved monoclonal antibodies that target HER2 in patients with confirmed Her2+ advanced or metastatic Gastric Cancer. In the Phase 1b dose finding part of the study tumor response of patients who received 50ug dose strongly correlated with antibody levels with 50ug selected as the Phase 2 dose (Wiedermann et. al., Annals of Oncology (2019)).

BACKGROUND

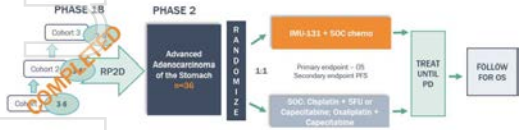

Figure 1: IMU.ACS.001 Study Design

In part 2 of study IMU.ACS.001, patients are randomized into two arms of either HER-Vaxx plus standard chemotherapy or standard chemotherapy alone.

The study is conducted in countries with limited access to trastuzumab in Asia and Eastern Europe.

The primary endpoint is overall survival, with progression-free survival and safety as secondary endpoints. Immune related endpoints include values and changes from randomization in humoral and cellular immunogenicity data.

METHODS

IMU-131 plus chemotherapy treated patients received 50ug dose of IMU-131 at Baseline/Day 0, Day 14, Day 35, Day 77 and then every 63 days until disease progression.

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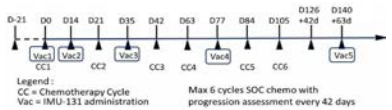

Figure 2: IMU.ACS.001 Phase 2 Treatment Schedule

RESULTS

Here we report the safety and efficacy results from the 1st interim analysis (OS and PFS) in a total of 27 patients after 15 progression events.

Within the ITT patient population, 8 of 27 patients have died on the control arm and 4 are deceased on the HER-Vaxx plus SOC chemotherapy arm. This translated into an overall survival HR of 0.418 (2 sided 80% CI: 0.186, 0.942) and a 1-sided p-value of 0.083. Progression free survival data of 27 patients was available, 9 patients progressed on the control arm and 6 patients on the HER-Vaxx plus SOC chemotherapy arm with a HR of 0.532 (2 sided 80% CI 0.267, 1.060) and a 1-sided p-value of 0.086.

Endpoint	Overall Survival Intent to Treat (Primary)		Progression Free Survival Intent to Treat (Secondary)	
Treatment	HERvaxx + Chemotherapy	Chemotherapy Only	HERvaxx + Chemotherapy	Chemotherapy Only
All Patients n=27	14	13	14	13
Events	4	8	6	9
HR	0.418		0.532	
2-sided 80%CI	(0.186,0.942)		(0.267,1.060)	
Log-rank Test (1-sided p-value) *	0.083*		0.086*	

*Pre-specified alpha at 0.10
* Statistically Significant

Table 1: IMU.ACS.001 Phase 2 Overall Survival & Progression Free Survival

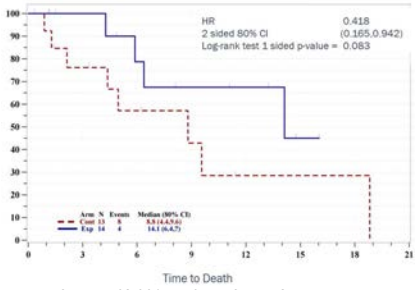

Figure 3 : IMU.ACS.001 KM-Curve Overall Survival Primary Endpoint

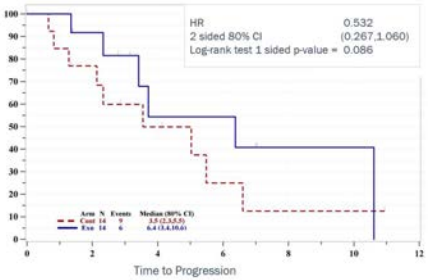

Figure 4: IMU.ACS.001 KM-Curve Progression Free Survival Secondary Endpoint

There was no difference in safety between the two treatment arms, suggesting HER-Vaxx does not add toxicity to SOC chemotherapy (Table 2).Incidence of Grade 3 and higher non-hematological (Table 3) and hematological adverse events (Table 4) were low and balanced between the treatment arms.

Two patients on each treatment arm had an asymptomatic LVEF drop, none of them below LVEF of 50.

Total (n=27)	HERvaxx + Chemotherapy n=14		Chemotherapy Only n=13	
	n	%	n	%
Patients with at least one TEAE	13	92.9%	12	92.3%
Grade 1	2	14.3%	3	23.1%
Grade 2	5	35.7%	2	15.4%
Grade 3	6	42.9%	4	30.8%
Grade 4	0		2	15.4%
Grade 5	0		1	7.7%

Table 2: IMU.ACS.001: Safety Overview of Treatment Emergent Adverse Events (TEAE)

Adverse Event ≥ Grade 3	HERvaxx + Chemotherapy n (grade)	Chemotherapy Only n (grade)
Gastrointestinal toxicity	0	1 (3)
Fatigue	2	0
Gamma-GT increased	2 (3+3)	0
Acute respiratory failure	1 (3)	1 (5)
Cachexia	0	1 (3)
Palmar-plantar erythrodysaesthesia syndrome	0	1 (3)
Pneumonia	0	1 (4)
Acute hepatic failure	0	1 (4)
Embolism	1 (3)	0
NOS (uncoded)	0	1 (3)
Total n	6	7

Table 3: IMU.ACS.001 Grade 3 and Higher Non- Hematological AE

Adverse Event	HERvaxx + Chemotherapy n	Chemotherapy Only n
Anemia:		
Grade 1+2	1	1
Grade 3	1	4
Febrile neutropenia:		
Grade 1	1	0
Neutrophil count decreased:		
Grade 2	1	0
Grade 3	1	0
Platelet count decreased:		
Grade 3	1	0
Grade 4	0	1
Total n	**6**	**6**

Table 4: IMU.ACS.001 Grade 3 and Higher Hematological AE

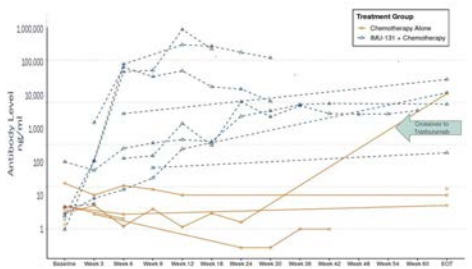

Figure 5: IMU.ACS.001 PHASE 2 - HER2 Specific Antibodies

By week 6 HER2-AB were developed by the patient's immune system as response to HER-Vaxx vaccinations and remained high during treatment with every 63 days maintenance vaccinations only. One patient on the chemo control arm progressed at week 24 and received trastuzumab containing treatment. The patient returned for one AB assessment that showed a similar level as HER-Vaxx (Figure 5).

Further data on response and biomarker is awaited.

CONCLUSIONS

These data demonstrate HER-Vaxx may provide treatment benefits consistent with traditional monoclonal antibodies with a corresponding adaptive immune response without toxicity.

A study (neoHERIZON) in perioperative HER2+GC with HER-Vaxx in combination with FLOT +/- anti-PD-L1 is in planning.

REFERENCES

Wiedermann et al: 2019, Annals of Oncology Volume 30 P495-496: Results of P1b study with a HER2/neu B-cell vaccine administered with chemotherapy in patients with HER2/neu overexpressing advanced gastric cancer

DISCLOSURES

Study is sponsored by Imugene Limited

B-cell peptide vaccine (IMU-131) was developed at the Medical University of Vienna

AACR Presentation

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Highlights

AACR

PFS Endpoint Events met on 21st April 2021: Top Line Data expected July 2021

Treatment with HER-Vaxx clearly demonstrates that all patients develop high levels of HER2-specific antibodies early in the treatment protocol.

Analysis of the antibody data reveals high levels are maintained during the treatment and maintenance phases, with only minimal booster injections of HER-Vaxx required to maintain the high levels.

The constant and high HER2 antibody levels correlate with the early separation of the Kaplan Meier (KM) Curves for overall survival (OS) and progression free survival (PFS) clinical trial endpoints. The Kaplan Meier Curve provides a recognised statistical estimation of the survival function which visually represents the probability of an event occurring for each treatment arm at a respective time interval.

Overall, this interim data is suggestive that the treatment is effective and well tolerated with an overall survival benefit that is superior to chemotherapy alone.

Final tumour response, correlation of antibodies with tumour response, and final PFS and OS data is expected to read out in 2021.

HER-Vaxx Phase 2: Interim Analysis

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ENDPOINT	OVERALL SURVIVAL Intent to Treat (Primary)		PROGRESSION FREE SURVIVAL Intent to Treat (Secondary)	
Treatment	Her-Vaxx + Chemotherapy	Chemotherapy Only	**Her-Vaxx + Chemotherapy**	**Chemotherapy Only**
All Patients N=27	14	13	14	13
Events	4	8	6	9
HR	**0.418**		**0.532**	
2-sided 80%CI	(0.186,0.942)		(0.267,1.060)	
Log-rank Test (1-sided p-value) *	0.083+		0.086+	

* Pre-specified alpha at 0.10
\+ Statistically Significant

HER-Vaxx Phase 2: Interim Analysis

TREATMENT EMERGENT ADVERSE EVENTS

	HER-VAXX + CHEMOTHERAPY (N=14)		CHEMOTHERAPY ONLY (N=13)	
Patients with at least one TEAE	**13**	**92.9%**	**12**	**92.3%**
	n	**%**	**n**	**%**
Grade 1 / 2	7	50%	5	38.5 %
Grade ≥ 3	6	42.9%	7	53.8%
Serious AE*	1	7.1%	5	38.5%
Fatal AE	0	0%	1	7.7%

*SAEs are also included in the ≥3 AE. N = number of patients in the treatment arm at interim analysis. n = number of patients who experienced the event.

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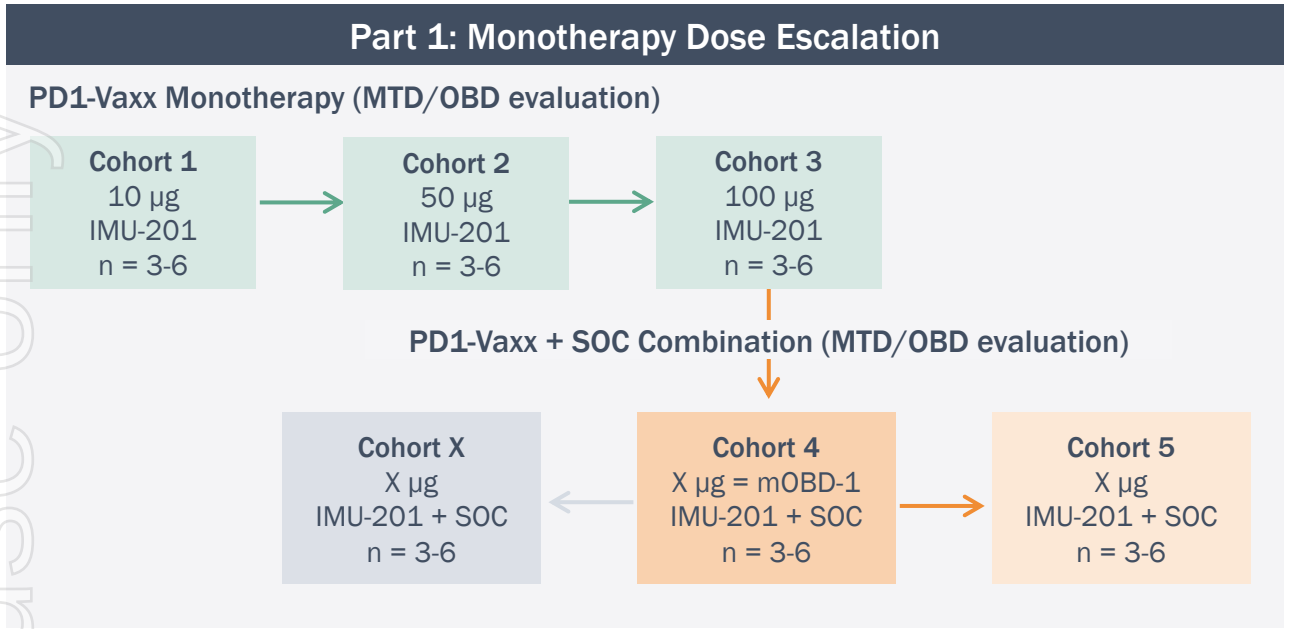
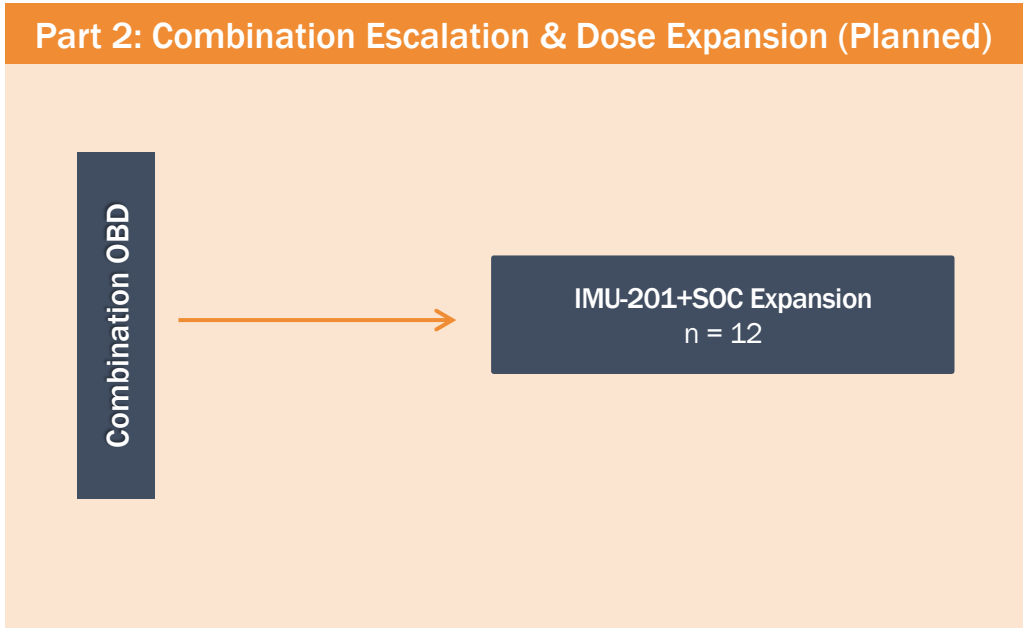
PD1-Vaxx

PD1-Vaxx Phase 1: Study Design





Phase	Part 1: Monotherapy Dose Escalation	Part 2: Combination Escalation & Expansion (Planned)
Indication	Non-small cell lung cancer expressing PD-L1	
Objectives	Safety & Tolerability, Immunogenicity, OBD Monotherapy	
No. of Patients	Approx. 12-22	Approx. 12-30
Site Location	Australia & USA	

PD1-Vaxx Phase 1: Recruiting

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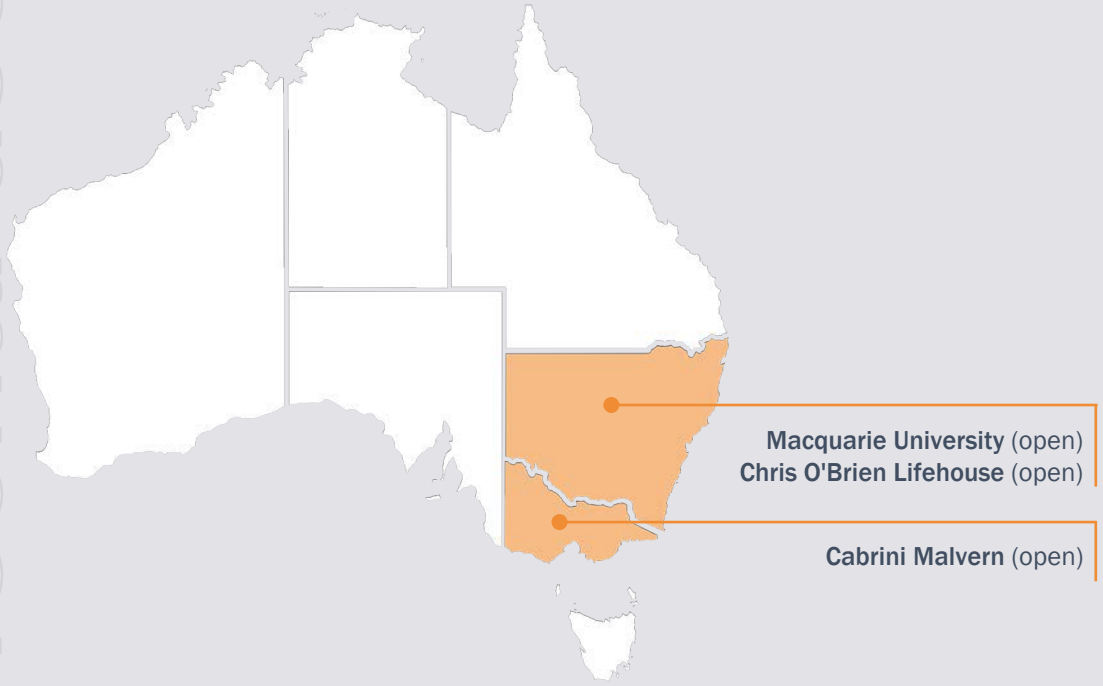
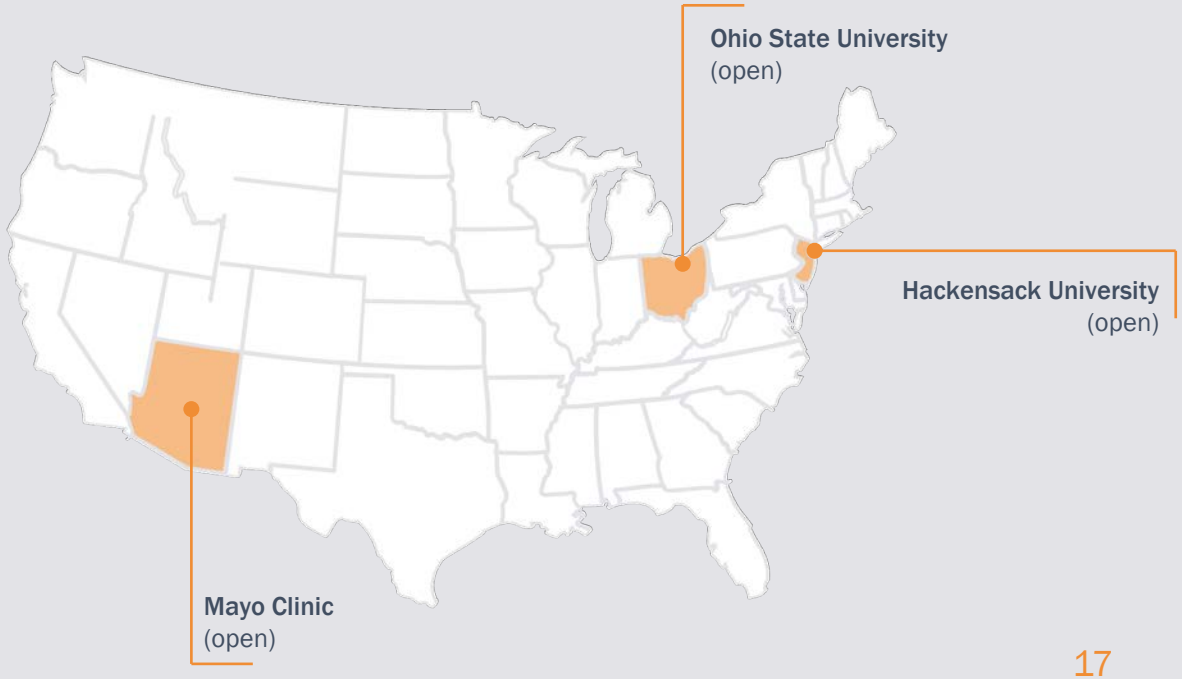
Current Status

MILESTONES

1st Patient Dosed Cohort 1	Cohort 1 Cleared	1st Patient Dosed Cohort 2	Cohort 2 Cleared	1st Patient Dosed Cohort 3	Cohort 3 Cleared, RP2D & Expansion Opened
30 Nov 2020	Jan 2021	Feb 2021	April 2021		





ESMO 2021 Presentation Poster

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2021 ESMO congress

Poster ID: 1367 TiP

IMPRINTER: An Open Label, Multi-Center, Dose Escalation/Expansion, Phase 1 Study of IMU-201 (PD1-Vaxx), a B-Cell Immunotherapy, in Adults with Non-Small Cell Lung Cancer

John Jae Won Park[1], Gary Richardson[2] , Martin Gutierrez[3], David Carbone[4], Michael Boyer[5], Panayiotis Savvides[6], Pravin Kaumaya[7], Tanios Bekaii-Saab[6], Tri Giang Phan[8], Leslie Chong[9], Rita Laeufle[9], Nicholas Ede[9], Bonnie NIxon[9], Anthony J. Good[9]

[1]Macquarie University Hospital, Sydney, Australia; [2]Cabrini Hospital Malvern, Melbourne, Australia; [3]Hackensack University Medical Center, New Jersey, NY; [4]The James Comprehensive Cancer Center, Columbus, OH; [5]Chris O'Brien Lifehouse Hospital, Sydney, Australia; [6]Mayo Clinic, Phoenix/Scottsdale, AZ; [7]Ohio State University, Columbus, OH; [8]St Vincent's Clinical School, UNSW, Sydney, Australia; [9]Imugene, Sydney, Australia,

Background

Therapies with monoclonal antibodies targeting PD-1 and its ligands are associated with remarkable outcomes in various cancers and, together with antibodies targeting CTLA-4, have revolutionized cancer treatment (Honey 2017). Some patients treated with PD-1/PD-L1 blockade may develop a "primary or secondary resistance" to therapy (Sharma, Hu-Lieskovan et al. 2017). The hypothesis is that a polyclonal induced B-cell antibody response will be more effective or as effective with improved safety over current monoclonal antibody therapy.

IMU-201 is being developed using an active immunization approach to treat cancers that overexpress programmed cell death ligand 1 (PD-L1) by inducing the production of anti-PD-1 antibodies through immunization of patients with a peptide epitope designed to stimulate polyclonal antibodies against PD-1 (Kaumaya et al. 2020).

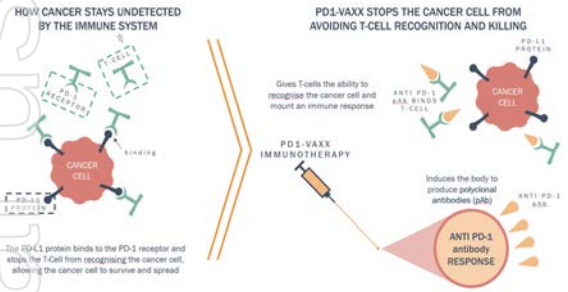

Figure 1, MOA of PD1-Vaxx

Study Description

The IMPRINTER study is an open-label dose escalation/dose expansion study of IMU-201 as monotherapy treatment for PD-L1 expressing lung cancer, to evaluate safety, tolerability, and immunogenicity and assess the optimum biological dose (OBD) of IMU-201 to be used for further clinical development. All patients enrolled in the study must have previously received an immune checkpoint inhibitor for their underlying cancer and experienced disease progression.

The study will continue into combination therapy that includes combination with SOC which may include a monoclonal AB (such as anti-PD-L1)

Study Design

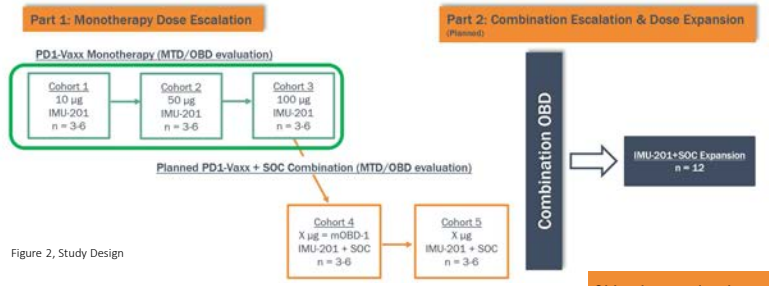

Figure 2, Study Design

Participating Countries and Sites

Figure 3 Map participating countries and sites

Treatment Regimen

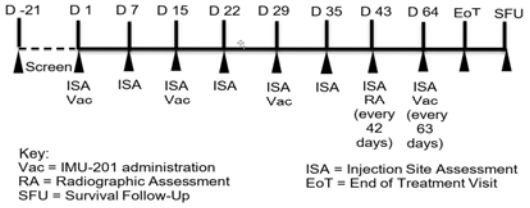

Figure 4, Vaccination schedule

Patient Selection

Histologically confirmed non-small-cell lung cancer (NSCLC) tumor stage IIIb or IV (3 major types of NSCLC are acceptable including squamous, adenocarcinoma, and large cell carcinoma);
Progressed on an approved PD-1 inhibitor or an approved PD-L1 inhibitor

Tumor PD-L1 overexpression with Tumor Proportion Score (TPS) ≥ 50%. Patients with PD-L1 TPS ≥ 1% expression may be included with agreement of Imugene Limited;

Objectives and primary Enpoints

Primary Objectives

- To evaluate safety/tolerability and immunogenicity of IMU-201 as monotherapy following treatment with PD-1 inhibitor or PD-L1 inhibitor therapy in patients with advanced NSCLC tumors that are positive for PD-L1.
- To identify the Optimal Biological Dose (OBD) of IMU-201 as monotherapy (mOBD), in patients with advanced NSCLC tumors that are positive for PD-L1.

Secondary Objectives

- To evaluate the efficacy of IMU-201 as monotherapy following treatment with SOC including monoclonal PD-1 inhibitor or PD-L1 inhibitor therapy in patients with advanced NSCLC tumors that are positive for PD-L1.

Exploratory Objectives

To evaluate changes in immunological, biomarker and additional radiological markers of tumor progression in patients treated with IMU-201 as monotherapy.

Primary Endpoints:

- Frequency of patients experiencing adverse events (AEs) graded by Common Terminology Criteria for Adverse Events (CTCAE) v5.0.
- Frequency of patients discontinuing study treatment due to AEs.
- The OBD of IMU-201 evaluated by safety/tolerability and immunogenicity data (IMU-201 and PD-1 specific antibody (IgG) titers).

Study Status

The study has fully enrolled into the third dose cohort, each cohort includes 3 patients. Treatment comprises 3 primary injections (days, 1, 15 and 29), a day 64 vaccination and from there a maintenance treatment every 2 months (see Figure 4). No dose limiting toxicity, or any significant vaccination related adverse event have been reported. Minor, grade 1 injection site reaction were reported with a duration of 1 day.

Overall, the treatment is well tolerated, and the study will therefore move into the expansion cohort enrolling 10 patients into the optimal biological dose, to confirm safety response and the development of PD1-antibody in correlation to response.

In planning is the combination with SOC therapy in the same patient population. This may include monoclonal AB such as a PD-L1 inhibitor or other immunotherapy agents. Patients may have either progressed on their previous therapy or lack of response to their SOC and are at high risk of progression .

Other tumor indication eligible for the treatment with immunotherapy are currently under evaluation.

REFERENCES

- **Honey, K. (2017).** "FDA Approves Fourth Immune Checkpoint Inhibitor for Bladder Cancer." Cancer Research Catalyst. The Offical Blof of the American Association for Cancer Research.
- **Sharma, P., S. Hu-Lieskovan, J. A. Wargo and A. Ribas (2017)**. "Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy." Cell **168**(4): 707-723.
- **Pravin T. P. Kaumaya, Linlin Guo, Jay Overholser, Manuel L. Penichet & Tanios Bekaii-Saab (2020)** Immunogenicity and antitumor efficacy of a novel human PD-1 B-cell vaccine (PD1-Vaxx) and combination immunotherapy with dual trastuzumab/pertuzumab-like HER-2 B-cell epitope vaccines (B-Vaxx) in a syngeneic mouse model, OncoImmunology, 9:1, DOI: 10.1080/2162402X.2020.1818437

Sponsor and Contact

Imugene Ltd, Australia, Contact via: info@imugene.com

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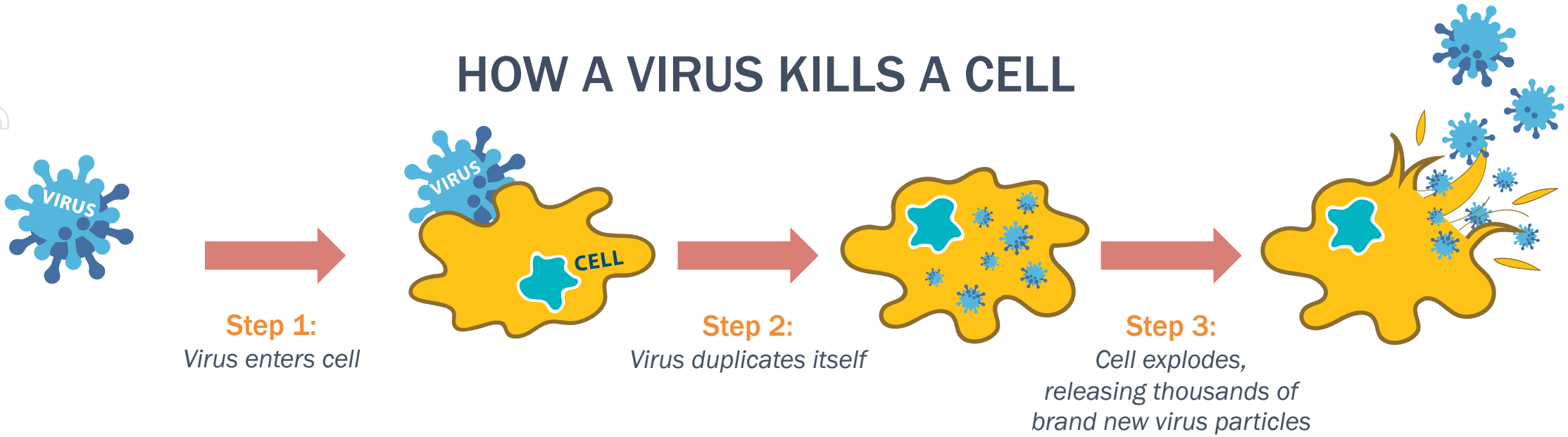
Developing Cancer Immunotherapies

Oncolytic Virus CF33

CF33 Mechanism of Action

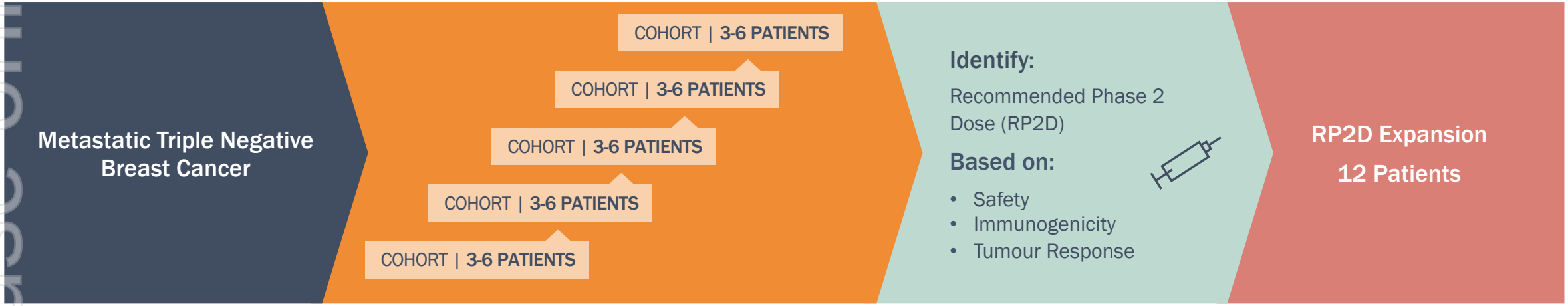


- Direct infection, replication within and cancer cell killing
- Viral infection increases local check point targets (PD-1, PD-L1, CTLA4 etc)
- Cell death is immunogenic [surface expression of calreticulin, release of adenosine triphosphate (ATP) and release of high mobility group box 1 (HMGB1)]
- Local anti-PD-L1 expression may allow enhancement of anti-cancer immunotherapy
- Human sodium iodine symporter (hNIS) expression allows additional use of ^{131}Iodine or ^{188}Rhenium killing of infected cells and adjacent cells

CHECKvacc Phase 1 TNBC Study

CF33+hNIS+aPD-L1 (“Armed” Virus)

FDA IND Cleared



Disease of need

- 8-13 month survival for metastatic disease with few treatments

Potential target for immunotherapy

- Expresses PD1, PD-L1

Treatment responses to Atezolizumab (JAMA Oncology, 5:74, 2019)

- 1st line: 24%; 2nd line: 6%
- Approved by FDA 8 March 2019

Potential for registration in well-designed, randomised P2 study

Indication	TNBC
FDA IND	CHECKvacc: CF33-hNIS-aPDL1
N	Part 1=18-24 ; Part 2=12
Location	Single Center: COH
Admin Route	Intratumoral (IT)

VAXINIA Phase 1 MAST Study
(Metastatic Advanced Solid Tumours)

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Dose Admin

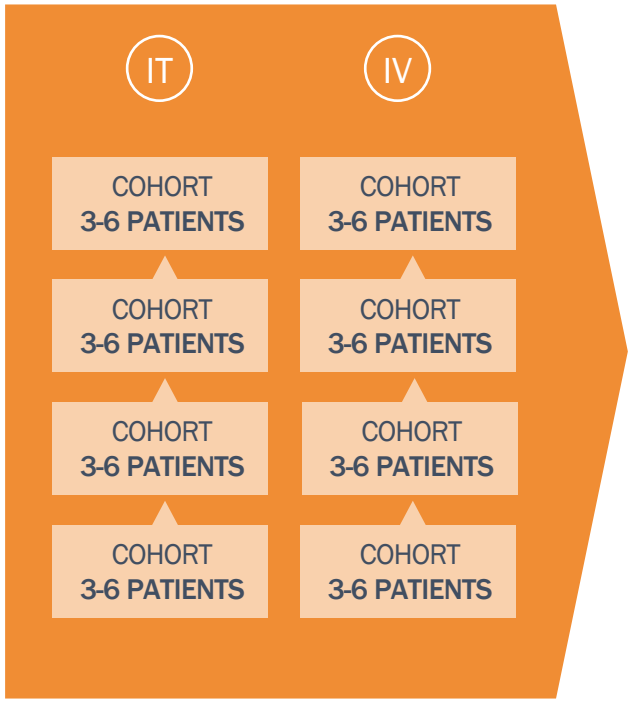
IT

IT Administration
Head & Neck, Advanced Melanoma, TNBC

IV

IV Administration
Head & Neck, Advanced Melanoma, TNBC, NSCLC, Bladder, Gastric, Colorectal, RCC

Part 1: VAXINIA Monotherapy Dose Escalation

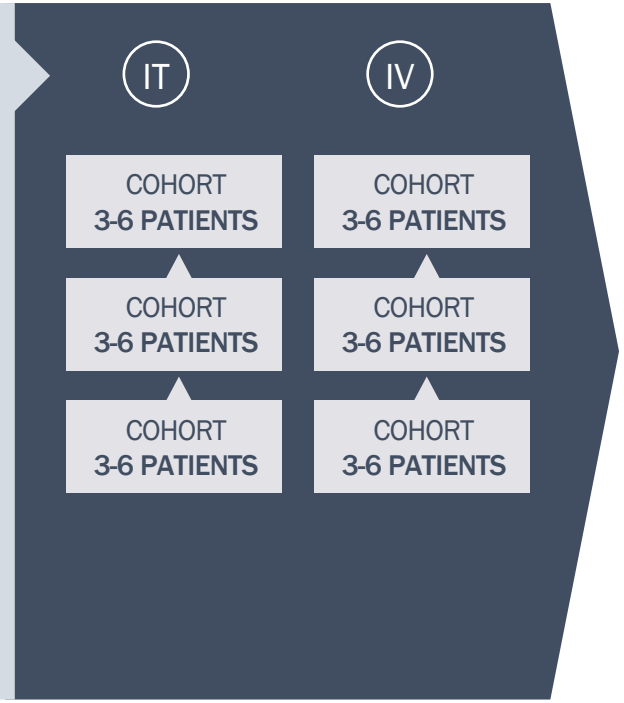


Identify Monotherapy

Maximum Feasible Dose (MFD), based on:

- Safety
- Immunogenicity
- Tumour Response

Part 2: VAXINIA + SOC IO* Combination Dose Escalation



Identify Combination

DLT# cleared VAXINIA monotherapy dose combined with IO* in dose escalation cohorts. Select IO* Combination for recommended phase 2 dose (RP2D) based on:

- Safety
- Immunogenicity
- Tumour Response

No. of Patients: Approx. 60-120
Site Location: USA

**IO: Immunotherapy*
#DLT: Dose Limiting Toxicity

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.

IMUGENE
Developing Cancer Immunotherapies

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 with onCARlytics (CF33-CD19) presents CD19 targets on solid tumours

Introducing onCARIytics

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

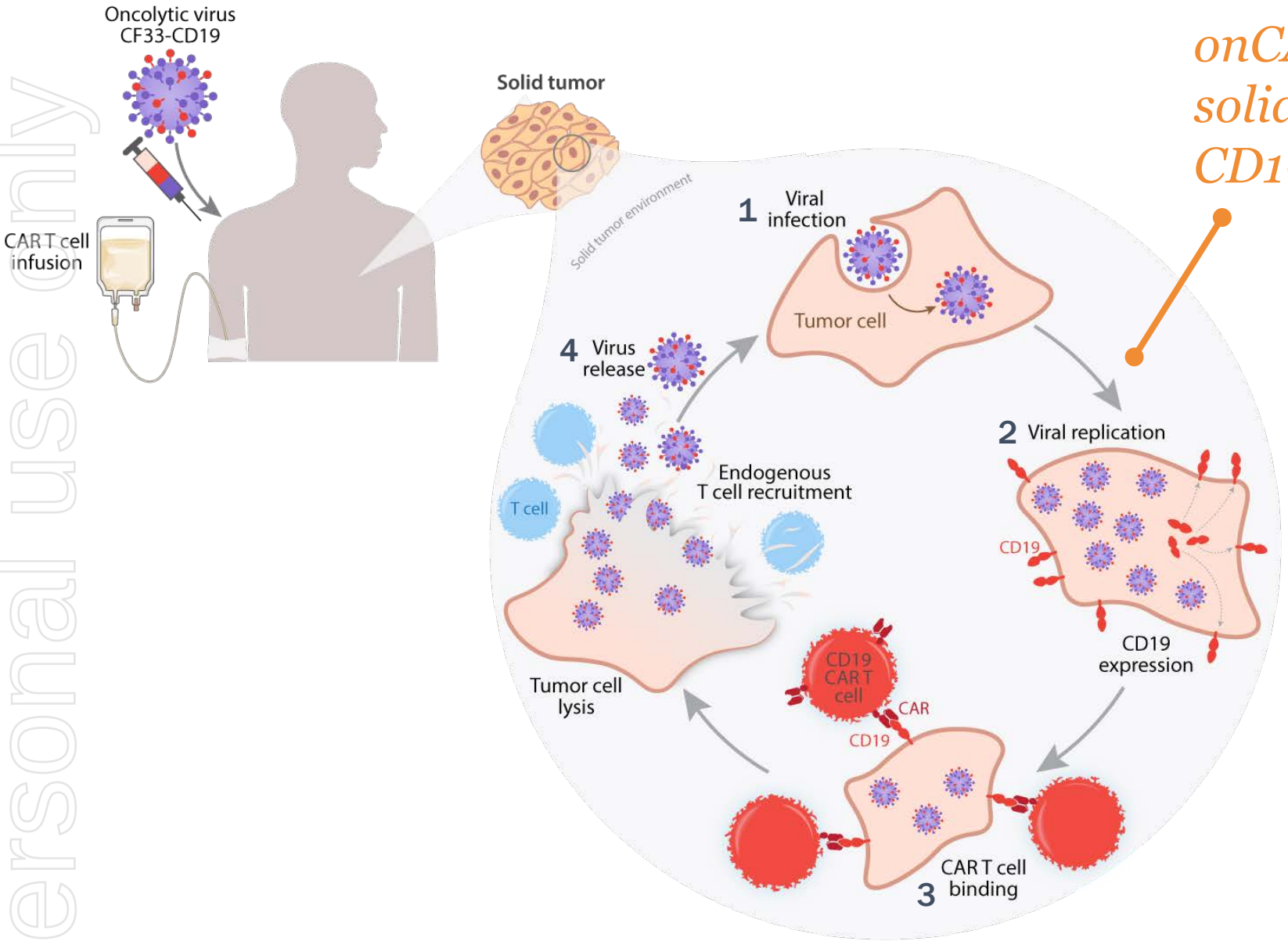
Dr Saul Priceman

Watch:
Combination CAR T Oncolytic Virus Immunotherapy Kills Tumours

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

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

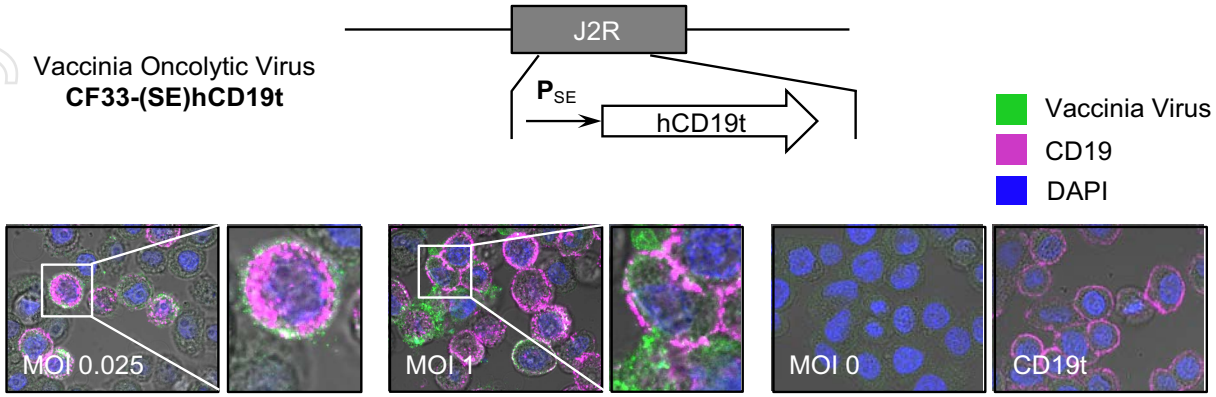
Mechanism of Action: How does it work?



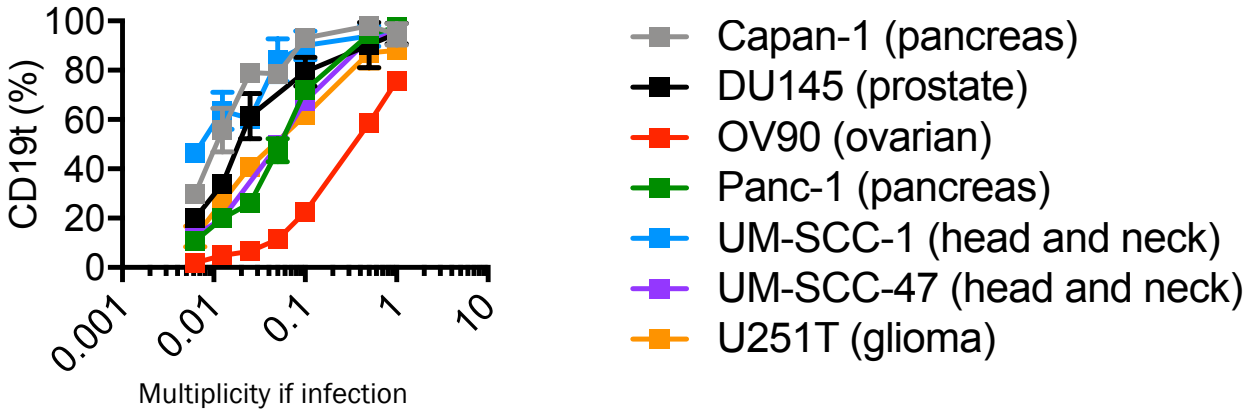
onCARlytics makes solid tumours "seen" by CD19 directed CAR T

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

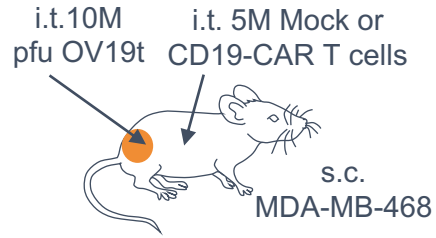


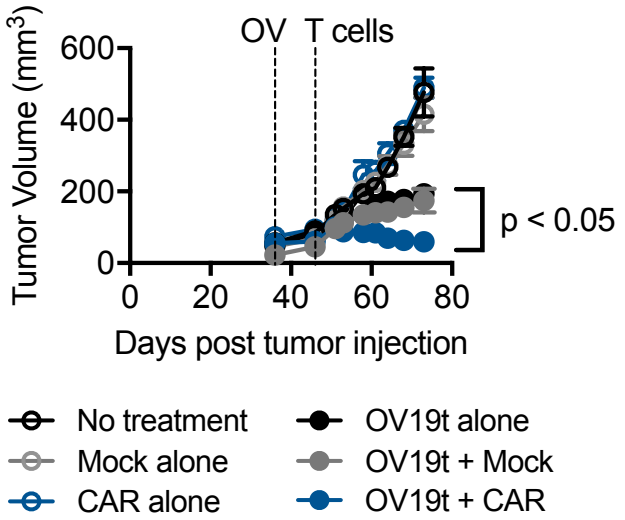
onCARIytics (CF33-CD19) infects a wide array of solid tumour cell lines, with dose-dependent CD19 cell surface expression



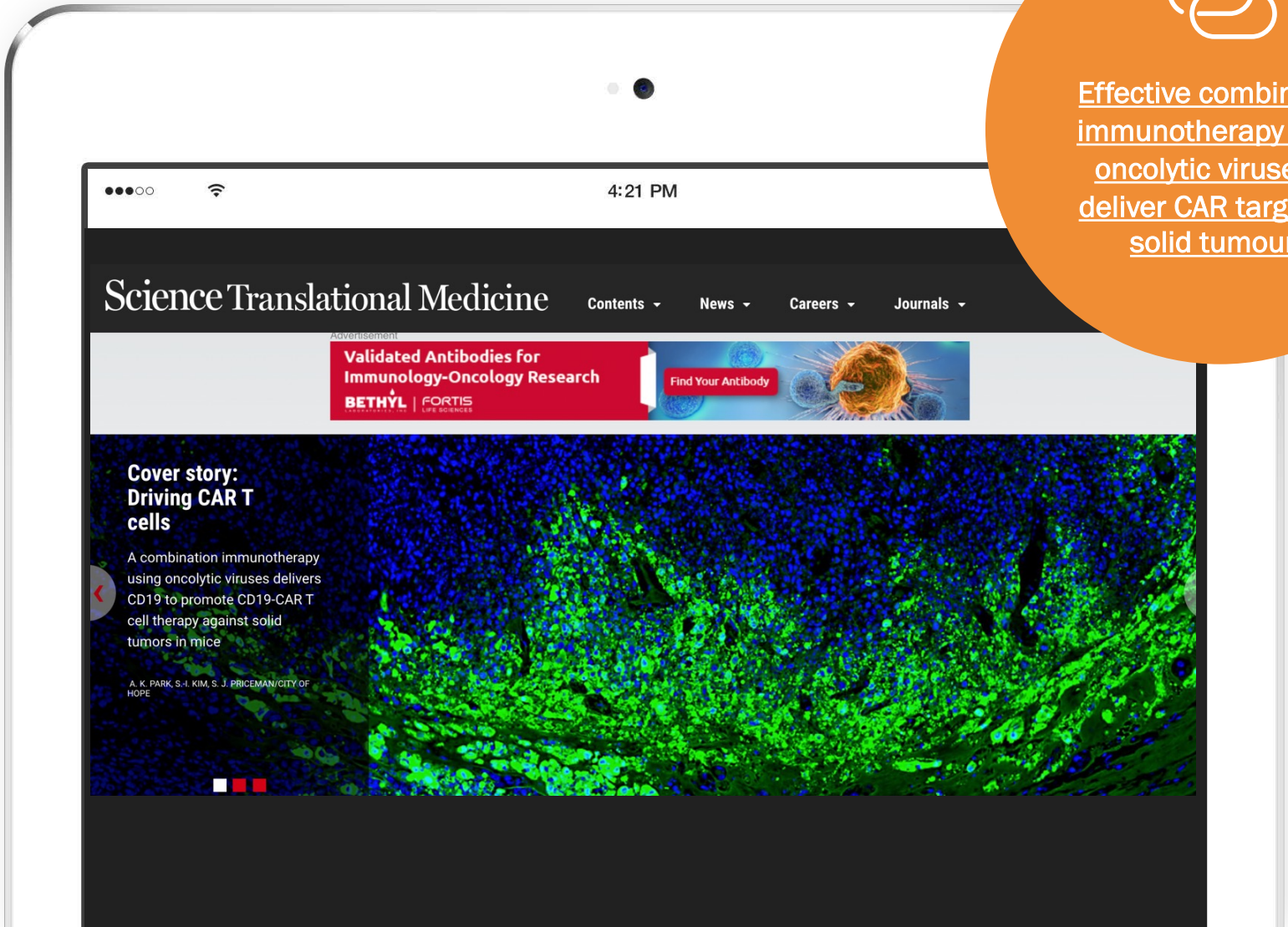
Park et al. *Science Translational Medicine* 2020

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





Published Front Cover of Science Translational Medicine Journal in 2020



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

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

Four FDA Approved CD19 CAR T's

IMUGENE
Developing Cancer Immunotherapies

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

Milestones

✓	Technology	Milestone
	onCARIytics	1st Patient Dosed
	onCARIytics	FDA IND Clearance
	PD1-Vaxx	Combination RP2D
	onCARIytics	GLP Toxicology Study
	VAXINIA	1st Patient Dosed
	onCARIytics	FDA Pre-IND Meeting
	onCARIytics	GMP manufacturing for pre-clinical toxicology & Phase 1 study
	VAXINIA	FDA IND Clearance
	HER-Vaxx	Neo and Next HERIZON studies
	PD1-Vaxx	Maximum Feasible Dose Identified
	HER-Vaxx	OS Primary Endpoint
	CHECKvacc	TNBC IST 1st Patient Dosed
✓	HER-Vaxx	PFS analysis data
✓	onCARIytics	Strategic partnership with Celularity on CD19 CART
✓	CHECKvacc	FDA IND Clearance

Next 12-24 months

Financial Summary

Public Market Overview

Share Price [1]	A$0.415
52 week range	0.052 - 0.515
Market Capitalisation [2]	A$2.43B
Cash equivalents (30 Jun 21)[3]	A$29.5M
Enterprise Value	A$2.538B

Top 5 Shareholders (as at September 2021)

Citicorp Nominees Pty Limited	5.96%
Richard Mann and Assoc.	5.35%
Paul Hopper	5.34%
HSBC Custody Nominees (Australia)	3.35%
Dr Nicholas Smith	2.16%

Note:
1. As of 22 Sep 2021
2. Market capitalisation calculations based on ordinary shares (5.46 bn) only and excludes the dilutive impact of options outstanding (0.64 bn)
3. Does not include 95m from capital raise and SPP

Share Price Performance (last 6 months)

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ASX: IMU

IMUGENE LIMITED

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info@imugene.com