

ASX: IMU

Developing Cancer Immunotherapies



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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
Licensed HERVaxx from the
Medical University
of Vienna

2017 HER-Vaxx enters the clinic 2019

Licensed CF33 oncolytic virus platform from City of Hope invented by Dr Yuman Fong 2021

Licensed on CARlytics from City of Hope invented by Dr Y Fong, Dr S Priceman & Dr A Park 2021

CHECKvacc enters the clinic 2021

HER-Vaxx Clinical
Trial Supply
Partnership with
Merck KGaA & Pfizer

2021

Entered the S&P/ASX 200 Index 2022

HER-Vaxx Phase 2 Final OS



EXPERIENCED MANAGEMENT TEAM WITH SIGNIFICANT CLINICAL DEVELOPMENT EXPERTISE

















THREE UNIQUE TECHNOLOGY PLATFORMS MAXIMIZE OPPORTUNITIES IN SOLID TUMORS

PLATFORM

TRIALS

CLINICAL



Therapeutic approaches with combination potential with existing standards of care

IMUGENE Developing Cancer Immunotherapies B Cell Immunotherapy onCARlytics IMUGENE CF33 Oncolytic Virus **CF33-CD19 CAR T Combination Therapy CHECKvacc VAXINIA HER-Vaxx PD1-Vaxx IP TO 2036 IP TO 2037 Granted in IP TO 2037 IP TO 2038** Filed in major territories multiple Filed in major Filed in major territories **Granted in Japan/Mexico** countries territories (US/EU/Asia) **COH TNBC IST** TBC **MAST HERIZON IMPRINTER** Phase 1 Phase 1 Phase 1 Phase 1b/2 Phase 1 celularity' **DOMINICA** nextHERIZON Phase 1 Phase 2 neoHERIZON Phase 2 TIGIT-Vaxx, PDL1-Vaxx, LAG3-Vaxx, 5 TIM3-Vaxx. CTLA4-Vaxx

5

IMUGENE'S DEEP IMMUNOTHERAPY PIPELINE FOR THE TREATMENT OF SOLID TUMORS



PLATFORM	PROGRAM/ TARGET	COMBINATION APPROACH	INDICATION	IND	PRECLINICAL	IND	PHASE 1	PHASE 2	2023 EXPECTED MILESTONES
onCARIytics IMUGENE	onCARlytics (CF33-CD19)	CD19 targeted therapies	Metastatic Solid Tumors		PHASE 1				FDA IND FPI
CF33 Oncolytic Virus	VAXINIA (CF33)	Pembrolizumab	Metastatic Solid Tumors	\bigcirc	MAST				IV Cohort 2 Cleared Optimal Biological Dose Combination FPI IT and IV Combination OBD IV
CF33 ONE (**) INJOETHE	CHECKvacc (CF33-aPD- L1)	Checkpoint Inhibitors	Metastatic TNBC	\Diamond	CHECKvacc IS	ST			IT Cohort 3 Cleared Optimal Biological Dose
	CHECKvacc (CF33-aPD- L1)	Checkpoint Inhibitors	Solid Tumors		DOMINICA				FDA IND
E Cell Immunotherapy	HER-Vaxx (HER2)	Chemotherapy Checkpoint Inhibitors	First Line Gastric Cancer		HERIZON				Publication and Presentation (ASCO GI)
			Neoadjuvant Gastric Cancer		neoHERIZON				CTA Clearance FPI
			Metastatic Gastric Cancer	\Diamond	nextHERIZO	V			ASCO GI TiP Interim Data Readout
	PD1-Vaxx (PD1) Chemothero Atezolizuma	Chemotherapy Atezolizumab	Metastatic NSCLC	\bigcirc	IMPRINTER				Combination FPI
			MSI High CRC		NeoPolem I	ST			CTA Clearance FPI

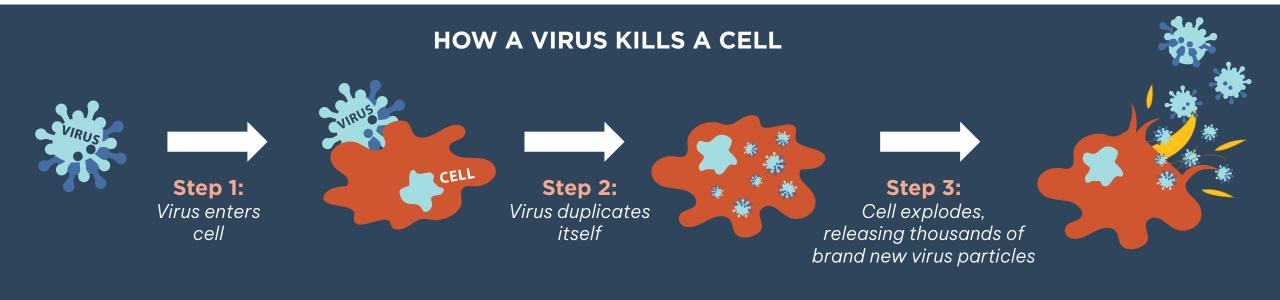


CF33 Oncolytic Virus



ONCOLYTIC VIRUSES OFFER A SELECTIVE IMMUNOGENIC APPROACH TO EFFECTIVELY KILL TUMOR CELLS





Engineering enhancements

- Infect and kill only cancer cells
- Carry additional payloads to augment killing (check point inhibitors, cytokines, antiangiogenics)

Multiple ways to kill cancer cells

- Direct Lysis
- Immuno-activation
- Priming of TME to enhance checkpoint inhibitor response¹

Precedent for approval

- Tvec approved in the United States for melanoma (2015)
- Oncorine approved in China for head and neck cancer (2005)
- Delytact approved in Japan for malignant glioma (2021)

MAJOR ADVANTAGES OF VAXINIA CF33





Robust Efficacy

Highly potent cancer killing

Converts 'cold' tumors to responsive 'warm' tumors

Direct intra-tumor and systemic anti-tumor activity

Well-Tolerated

Large therapeutic window

Genetically stable

Combinability with targeted therapies

Broad Application

Tumor agnostic approach

IT, IV or IP administration with potential to multi-dose

Combination approaches

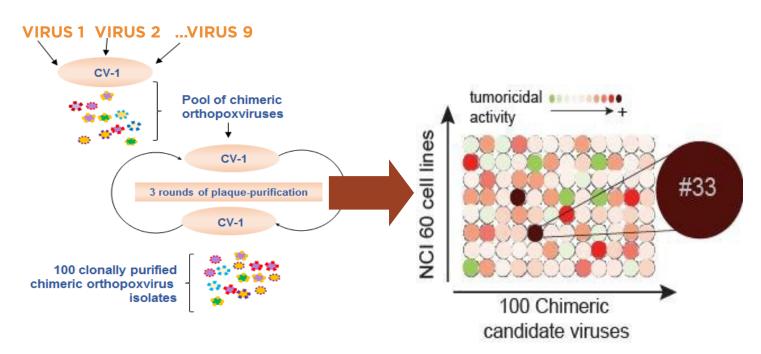
Scalability

Made in high titers

Storage stability

Clinically stable after mixing

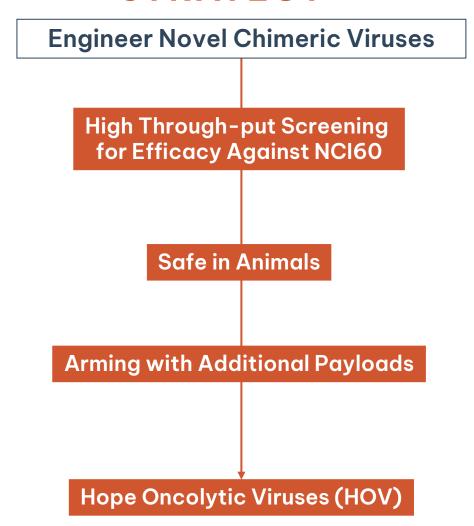
CF33 GENERATION & EVALUATION OF NOVEL CHIMERIC POXVIRUSES



- Infection by 9 different pox vaccinia vaccine strains trading genetic material isolating over 100 different clones (new species)
- Placed in the State-of-the-art high throughput screening for efficacy against the NCI 60 cell lines.
- The 33rd virus was chosen for its eradication of all cancer cell lines in the NCI 60, CF33



STRATEGY

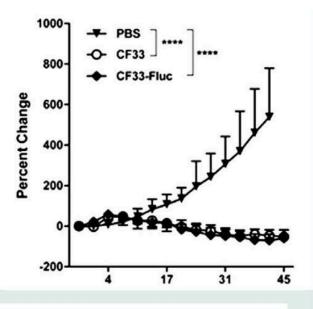


COMPELLING KILLING OF MANY TUMOR TYPES

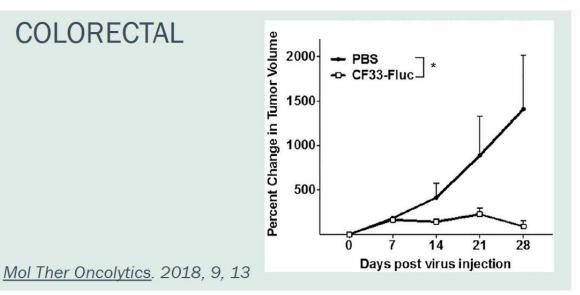


PANCREATIC

AT LOW DOSES

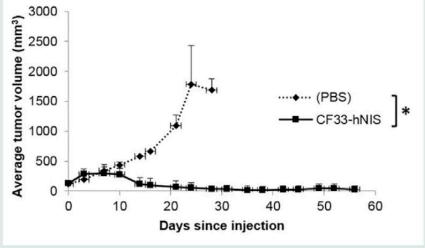


COLORECTAL

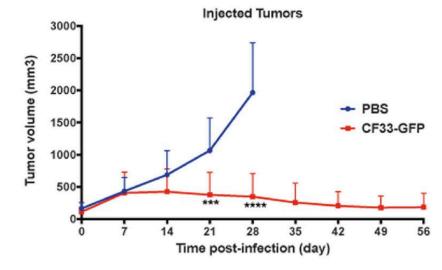


J Transl Med. 2018, 16, 110

COLON



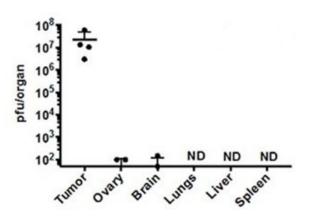
LUNG



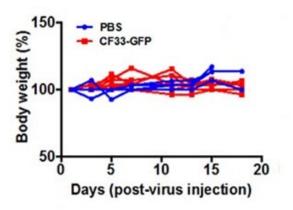
SAFELY DELIVERED ROUTES: IT, IP, IV ENABLES LARGE THERAPEUTIC INDEX IN PATIENTS



Tumor restricted viral delivery



No change in body weight



No toxicity across tumor models in over 1,000 mice until over 10⁹

VIRUS	MOUSE	# OF MICE	DOSE	DELIVERY	TOXICITY
CF33-NIS	Nude	73	1e3-1e5	IT	No findings
CF33-miR	Nude	41	1e3-1e5	IT	No findings
CF33-Luc	Nude NSG	48 8	1e3-2e5 1e6	IT, IV & IP IT	No findings
CF33-GFP	Nude NSG	18 8	1e3-2e7 1e6	IT IT	No findings
CF33-hNIS- αPDL1	Nude Black/6 BALB/c	52 67 31	1e4 1e5-1e8 1e7	IT IT & IV (1e6) IT & IV	No findings
CF33-hNIS- Δ14.5	Nude Black/6 BALB/c	36 16 16	1e4 1e6 – 1e8 1e7-3e7	IT IT IT & IV (2e7)	No findings
CF33-CD19	NSG	288	1e6-1e8	IT	No findings

Majority of mice cured with a single injection of 1000 pfu via IT, IV and IP delivery

CF33-hNIS: TUMOR TRACKING AND TROPISM



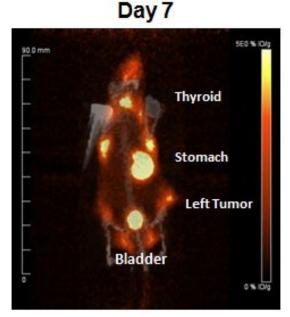
Genetic modification enables tumor tracking and tumor tropism

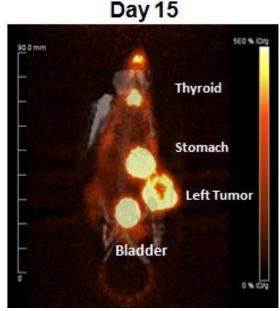
- hNIS (human sodium iodide symporter) protein is expressed on the tumor cell surface
- hNIS transgene inserted within J2R locus (Tk) to transport radioactive iodine for imaging

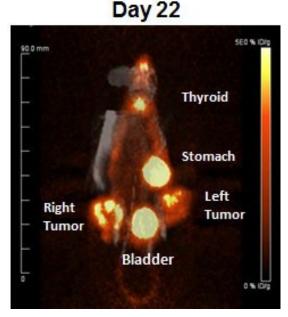
Tracked virus supports tumor specificity and systemic delivery

- Cross infection of tumors supported by 124l uptake in right side on day 22 following injection on left side
- Physiologic uptake in thyroid, stomach and bladder

124| PET Imaging of CF33-hNIS-infected HCT116 (colon cancer) from flank xenografts in nude mice over time







CHECKvacc PHASE 1 TNBC STUDY CF33+hNIS+aPD-L1 ("Armed" Virus)





Presented at SABC 2022

Identify: COHORT 8 | 3-6 PATIENTS **Metastatic Triple** Recommended Phase 2 **Negative Breast** • • • Dose (RP2D) **RP2D Expansion** Cancer Based on: 12 Patients COHORT 2 | 3-6 PATIENTS Safety - 2 prior lines of treatment Immunogenicity COHORT 1 | 3-6 PATIENTS • Tumor Response

First Patient Enrolled October 2021

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, randomized P2 study

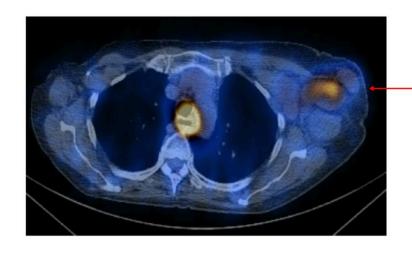
ndication	TNBC		
FDA IND	CHECKvacc: CF33-hNIS-aPDL1		
٧	33-78		
_ocation	Single Center: COH		
Admin Route Intratumoral (IT)			

CHECKvacc (CF33-hNIS-antiPD-L1) TUMOR TRACKING



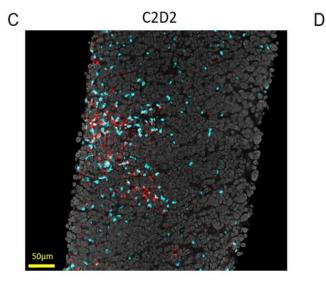






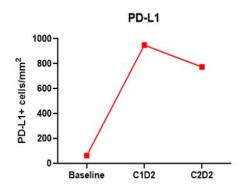
SPECT imaging of patient using Technetium-99m (C1D8): Patient COH-004 received CHECKvacc at Dose Level 2 (3x10⁵ PFU). Injected lesion was left axilla showed significant enhancement of injected lymph node.

hNIS 99m uptake in SPECT scan



SAN ANTONIO BREAST CANCER SYMPOSIUM

> Immune activationincrease in PD-L1



Multiplex immunofluorescence (mIF) of COH-004 tumor: C&D immune infiltrates shows increase density of PD-L1+ cells across patient tissue biopsies.

VAXINIA PHASE 1 MAST STUDY

COHORT

3-6 PATIENTS

COHORT

3-6 PATIENTS

COHORT

3-6 PATIENTS

3-6 PATIENTS

(Metastatic Advanced Solid Tumors)



Dose Administration (Parallel Groups)

n=52-100



IT Administration

Metastatic and Advanced Solid Tumors



IV Administration

Metastatic and Advanced Solid Tumors

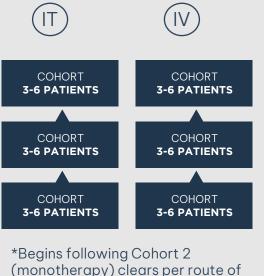
Site Location: USA, AUS

First Patient Enrolled May 2022, IV Cohort 1 Cleared Nov 2022

VAXINIA Monotherapy
Dose Escalation

VAXINIA + Pembrolizumab
Combination Dose Escalation*

Cohort Expansion



administration

RP2D Expansion (N=10)

Tumor Types of Interest

(cleared cohorts)

Identify: Recommended Phase 2 Dose (RP2D) – Monotherapy and Combination **Based on:** Safety, Immunogenicity, Tumor Response

COHORT

3-6 PATIENTS

COHORT

3-6 PATIENTS

COHORT

3-6 PATIENTS

3-6 PATIENTS



CF33-CD19



THE CELL THERAPY SOLID TUMOR CHALLENGE & IMUGENE'S SOLUTION

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

CD19 Targeting

Cells

Solid Tumor

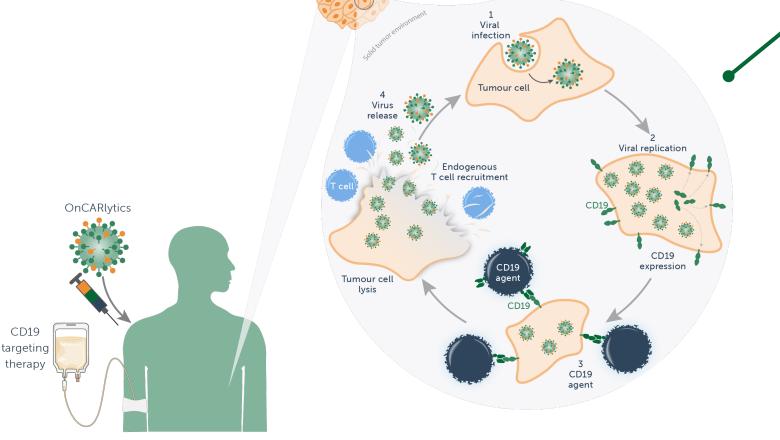
CD19 Targeting domain

> OV generated CD19

IMUGENE'S APPROACH

- Use onCARlytics (CF33-CD19) to express CD19 antigen on solid tumor cells
- Combine on CARlytics (CF33-CD19) with autologous or allogeneic CD19 CAR T cell therapies for the treatment of solid tumors

MECHANISM OF ACTION: HOW DOES IT WORK?



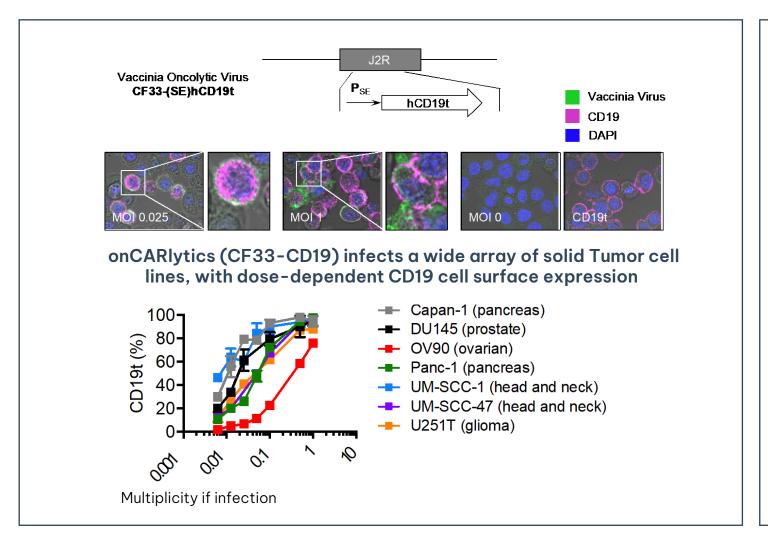
Solid tumour

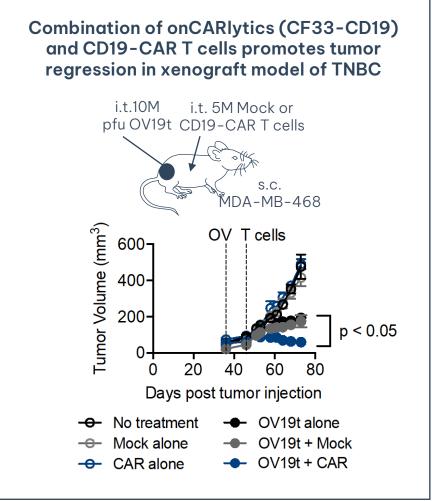
onCARlytics makes solid tumors "seen" by CD19 targeting therapies

- OnCARlytics infects Tumor cells
- 2. Virus replication and production of CF33-CD19 on the cell surface enabling CD19 cell targeting
- 3. Tumor cell lysis leads to viral particle release and the combination promotes endogenous immune cell recruitment to Tumors
- 4. Released viral particles reinitiate virus infection of surrounding Tumor cells.

onCARLYTICS DELIVERS TARGETS TO "TARGETLESS" SOLID TUMORS

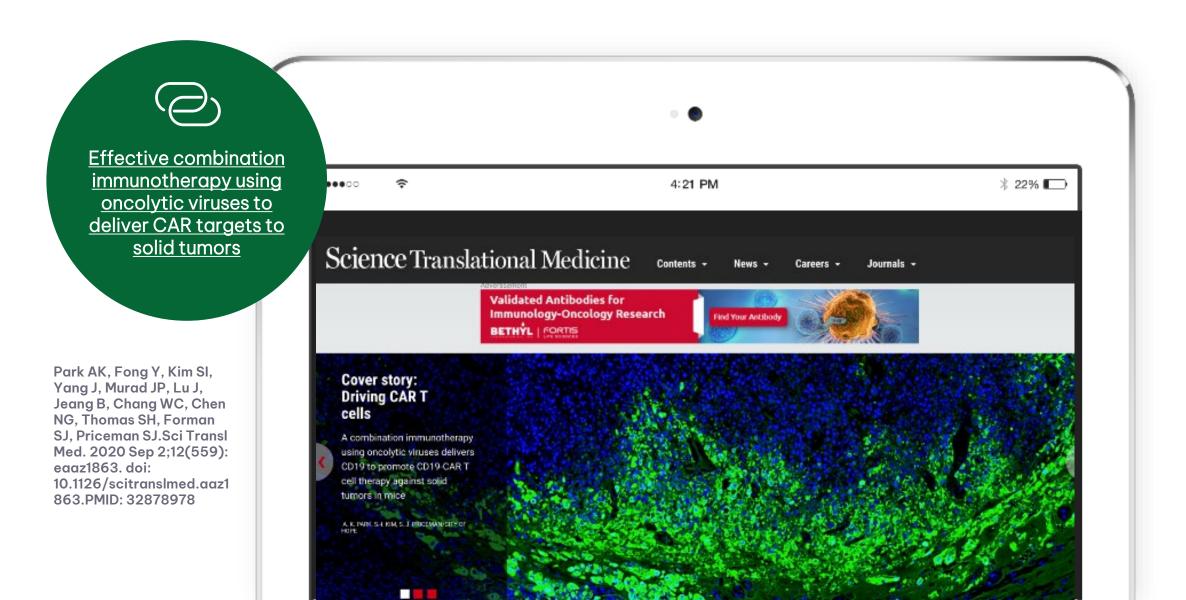






PUBLISHED FRONT COVER OF SCIENCE TRANSLATIONAL MEDICINE JOURNAL IN 2020

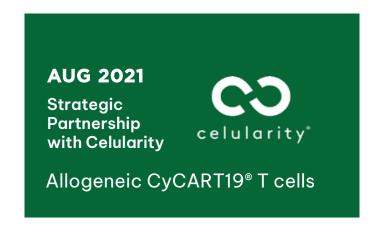




onCARLYTICS COMBINATION WITH CD19 TARGETING THERAPIES



Collaboration with Celularity, Eureka and Arovella for combination with onCARlytics





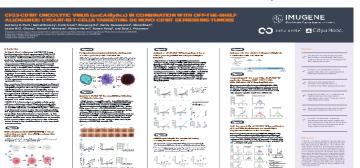




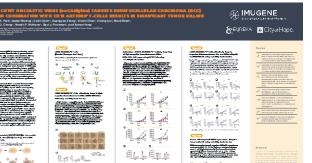
3 POSTERS PRESENTED AT SITC 2022



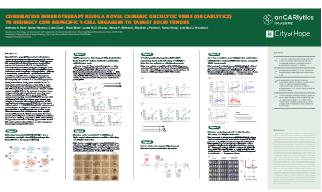














HER-Vaxx



B CELL BASED ANTIBODIES HAVE DISTINCT COMPETITIVE ADVANTAGES TO EXISTING TREATMENTS

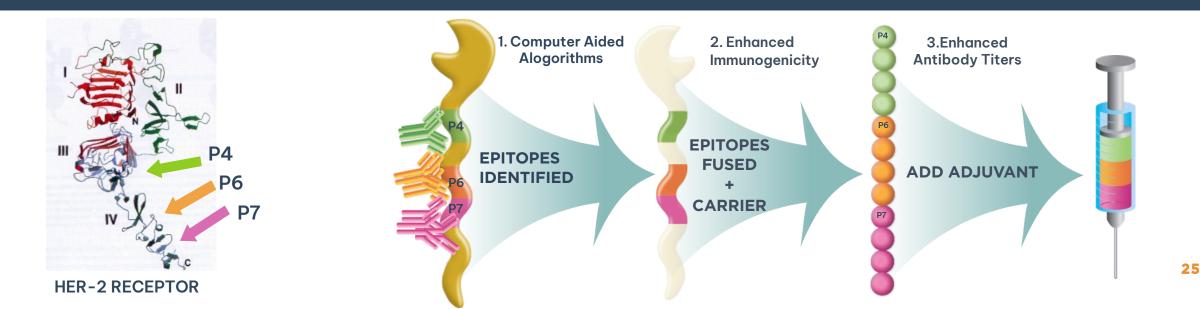


B cell vaccines offer a unique opportunity to intervene at multiple points in the immune system and create immune memory which enhances durability of response.	NATURAL B CELL DERIVED ANTIBODIES	MONOCLONAL ANTIBODIES
Safety	Stimulates the immune system to produce Abs, which may be potentially safer	Synthetic Ab, with side effects (including ventricular dysfunction, CHF, anaphylaxis, infusion reactions, 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	After priming, 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: B-CELL IMMUNOTHERAPY VACCINE AGAINST HER-2

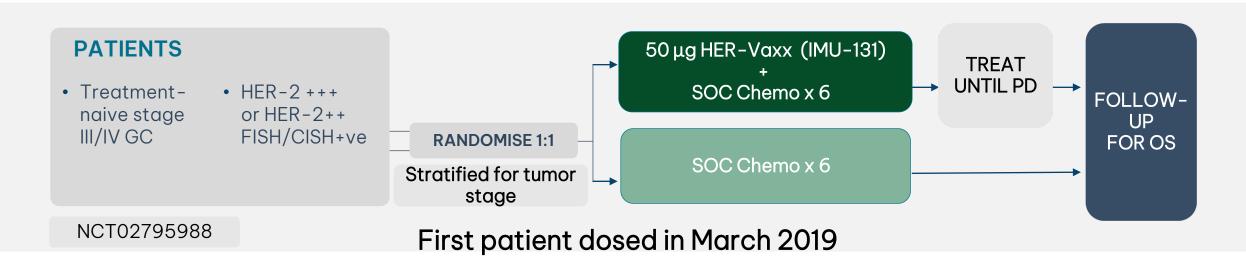


- B-cell cancer vaccine designed to stimulate a patient's own immune system to repeatedly target the HER-2+ cancer with HER-2 directed antibodies
- Stimulates a patient's B cells to produce polyclonal antibodies that target cells with overexpressing HER-2 receptors on their surface
- HER-Vaxx consists (1) of three fused B-cell epitope peptides (P4, P6, P7) from the HER-2 receptor conjugated to (2) a carrier protein CRM197 plus (3) an adjuvant Montanide ISA51. Injected as a water-in-oil emulsion.



HERIZON PHASE 1B/2 OPEN LABEL, MULTICENTER STUDY





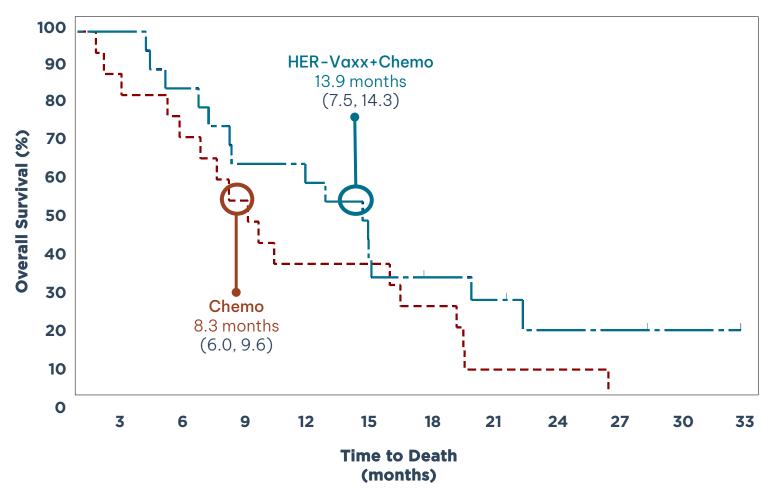
HER-Vaxx	C1D1, C3D1 then Q9 weeks till PD					
Chemotherapy	6 cycles Q3 weeks (Cisplatin + 5FU or	6 cycles Q3 weeks (Cisplatin + 5FU or Capecitabine; Oxaliplatin + Capecitabine)				
PRIMARY ENDPOINT	OS (pre-spec 1-sided alpha 0.10, power 90% with critical HR 0.6 and 24 events)	NO. OF PATIENTS 3	6			
SECONDARY ENDPOINTS	PFS, Safety, Immune Response	SITE LOCATION E	astern Europe, India			







HER-Vaxx SIGNIFICANTLY PROLONGS OVERALL SURVIVAL IN 1L PATIENTS WITH HER-2+ GASTRIC CANCER



	HER-Vaxx + Chemotherapy	Chemotherapy
Sample Size	19	17
Events	15	17
Median OS	13.9 months	8.3 months
(2-sided 80% CI)	(7.5, 14.3)	(6.0, 9.6)
Median Duration of Response	30 weeks	19 weeks
HR	0.5	80
2-sided 80%Cl	(0.362, 0.927)	
Log-rank Test (1-sided p- value) *	0.066 *	

^{*}Significant, 1-sided p < 0.10

HER-Vaxx PHASE 2:HERIZON SAFETY



TREATMENT EMERGENT ADVERSE EVENTS

	HER-Vaxx + CHEMOTHERAPY (N =1 9)	CHEMOTHERAPY ONLY (N =1 7)	
	n (%)	n (%)	
Patients with at least one TEAE	18 (94.7%)	16 (94.1%)	
Grade 1 / 2	10 (52.6%)	9 (52.9%)	
Grade <u>></u> 3	8 (42.1%)	7 (41.2%)	
Serious AE*	2 (10.5%)	5 (29.4%)	
Fatal AE	1(5.3%)	1(5.9%)	

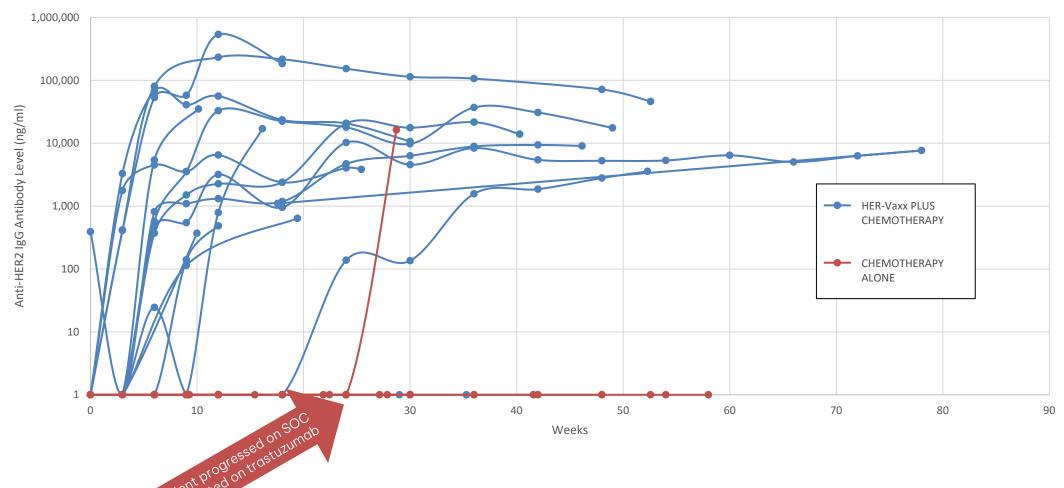
^{*}SAEs are also included in the \geq 3 AE. N = number of patients in the treatment arm at final analysis. n = number of patients who experienced the event.

HER-Vaxx PHASE 2:

HERIZON HER-2 ANTIBODY LEVELS PER PATIENT



HER2-Specific IgG by Treatment Assignment and Study Visit - Logarithmic Scale



HER-Vaxx PHASE 2: nextHERIZON IN METASTATIC GASTRIC CANCER AFTER PROGRESSION ON TRASTUZUMAB













- Phase 2
- Open label
- USA, Australia, Asia
- Treat until progression/toxicity

- > 1L
- Advanced or metastatic Gastric Cancer
- HER-2/neu overexpressing
- Progressed on prior trastuzumab
- Non-Randomised
- HER-Vaxx in combination with paclitaxel + ramucirumab OR
 - HER-Vaxx in combination with pembrolizumab

Primary

- Objective Response Rate
- Safety

Secondary

- Overall Survival
- Progression-free survival
- Duration of Response

First Patient Enrolled Sept 2022

mGC/GEJ cancer
HER-2/neu overexpressing
Progressed on or after trastuzumab &
previously received PD-1/PD-L1 treatment

Arm 1: HER-Vaxx + SOC Chemotherapy

mGC/GEJ cancer
HER-2/neu overexpressing
Progressed on or after trastuzumab

Arm 2: HER-Vaxx + pembrolizumab

PRIMARY ENDPOINTS:

ORR Safety

SECONDARY ENDPOINTS:

OS PFS DoR

EXPLORATORY ENDPOINT: Biomarker/Immune Response

HER-Vaxx PHASE 2: neoHERIZON IN RESECTABLE GASTRIC CANCER











- Phase 2
- Open label
- Randomised
- Germany

- Neoadjuvant Gastric Cancer
- HER-2++/HER-2++ FISH/CISH+ve

- Arm 1 FLOT + HER-Vaxx
- Arm 2 FLOT + Avelumab + HER-Vaxx

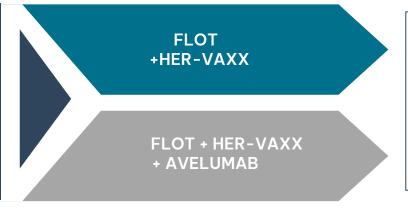
Primary

• Pathological Complete Response

Secondary

- Safety
- Immune Response
- Duration of Response/Overall Survival

Resectable HER2 overexpressing Gastric & GEJ cancer





PRIMARY ENDPOINTS: pCR

SECONDARY ENDPOINTS: Safety, Immune response, DoR/OS

> EXPLORATORY ENDPOINT: Biomarkers



PD1-Vaxx



PD1-VAXX STOPS CANCER CELLS FROM USING PD1 TO STAY UNDETECTED BY THE IMMUNE SYSTEM



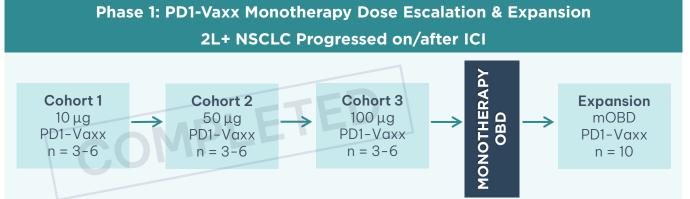
PD-L1 binding to PD-1 prevents T cell recognition and killing of cancer cells binding Cancer Cell Protein Cancer cells express PD-L1 which binds to the PD-1 receptor on T cells

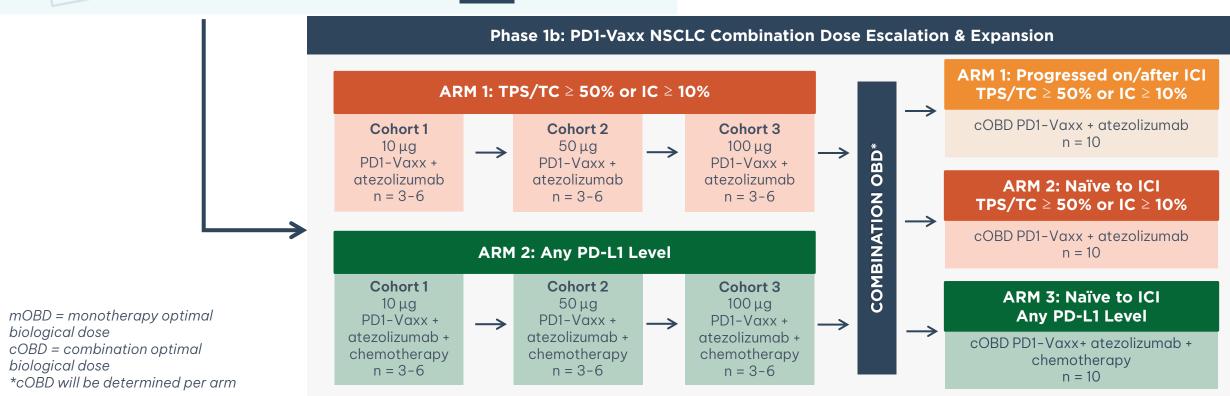
PD1-Vaxx stops cancer cells from staying undetected by T cells PD1-VAXX B cell vaccine ANTI PD-1 pAb Anti-PD1 pAb binds PD1 on the T cell PD-L1 PROTEIN Anti-PD1 pAb Induces the body to blocks PD-L1 produce polyclonal antibodies (pAb) interaction on cancer cell Cancer Cell T cells recognize cancer cells and mount an 33

immune response

IMPRINTER: PD1-Vaxx NSCLC PHASE 1 STUDY DESIGN







VALUE INFLECTION POINTS EXPECTED IN THE NEXT 12 MONTHS



TECHNOLOGY MILESTONE VAXINIA MAST: Combination OBD IV onCARIytics FPI HER-Vaxx neoHERIZON: FPI HER-Vaxx nextHERIZON: Interim Data Readout **VAXINIA** MAST: Optimal Biological Dose (Monotherapy IV and/or IT) HER-Vaxx neoHERIZON: CTA Clearance **CHECKvacc** Dominica: FDA IND **CHECKvacc** COH IST: Optimal Biological Dose PD1-Vaxx IMPRINTER: Combination FPI onCARlytics FDA IND **CHECKvacc** COH IST: IT Cohort 3 Cleared **VAXINIA** MAST: Combination FPI IT and/or IV **VAXINIA** MAST: IV Cohort 2 Cleared HERIZON: Publication and Presentation (ASCO GI) HER-Vaxx HER-Vaxx nextHERIZON: Trial in Progress Poster (ASCO GI) VAXINIA MAST: IV Cohort 1 Cleared onCARIytics Strategic Partnership with Arovella on CAR19-iNKT VAXINIA MAST: IV Arm - 1st Patient Dosed HER-Vaxx nextHERIZON: Phase 2 - 1st Patient Dosed HER-Vaxx HERIZON: Phase 2 Final OS readout

NEXT 1-12 MONTHS

FINANCIAL SUMMARY



PUBLIC MARKET OVERVIEW (January 4, 2023)

Share Price	A\$0.155
52 week range	\$0.13 - \$0.43
Market Capitalisation ¹	A\$995M
Cash equivalents (30 September '22)	A\$164M
Enterprise Value	A\$831M

TOP 5 SHAREHOLDERS (as at January 4, 2023)

9.24%
5.69%
4.94%
4.60%
4.58%

SHARE PRICE PERFORMANCE



Note:

^{1.} Market capitalisation calculations based on ordinary shares (6.422 bn) only and excludes the dilutive impact of options outstanding (0.477 bn)

INVESTMENT HIGHLIGHTS



MARKET CAPITALISATION 4th Jan 2023

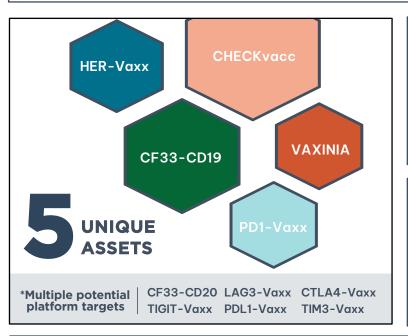
A\$995M

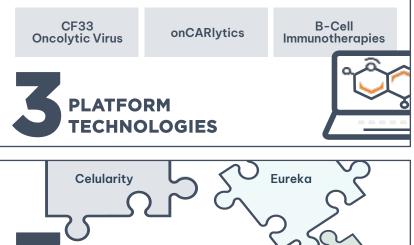


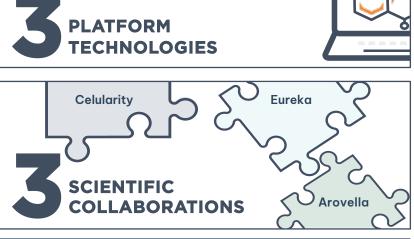
CASH AS OF 30th Sep 2022

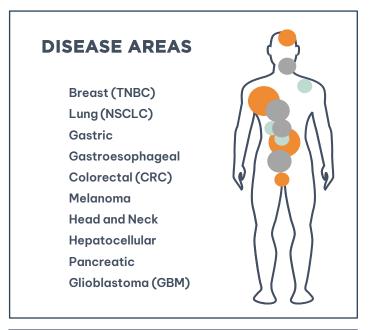
A\$164M













CLINICAL STUDIES

HERIZON: Ph1b/2 First line Gastric Cancer IMPRINTER: Ph1 NSCLC (FDA IND) CHECKvacc COH IST: Ph1 TNBC (FDA IND) neoHERIZON: Ph 2 Neoadjuvant Gastric Cancer

nextHERIZON: Ph2 Metastatic Gastric Cancer (FDA IND)

MAST: Ph1 Solid Tumors (FDA IND) DOMINICA: Ph1 TNBC (FDA IND)

onCARlytics: Ph1 Solid Tumors (FDA IND)

neoPolem IST: Ph1 CRC





Merck KGaA/Pfizer

Roche

Contact

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