



**IMUGENE**  
Developing Cancer Immunotherapies

ASX: IMU

# IMUGENE

Investor Presentation

November 2020

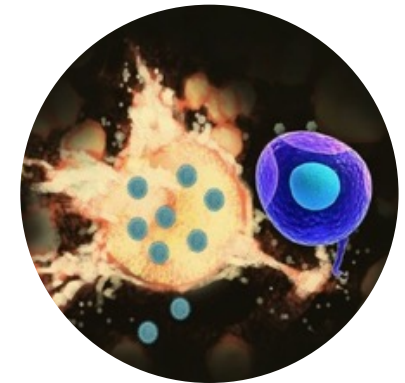
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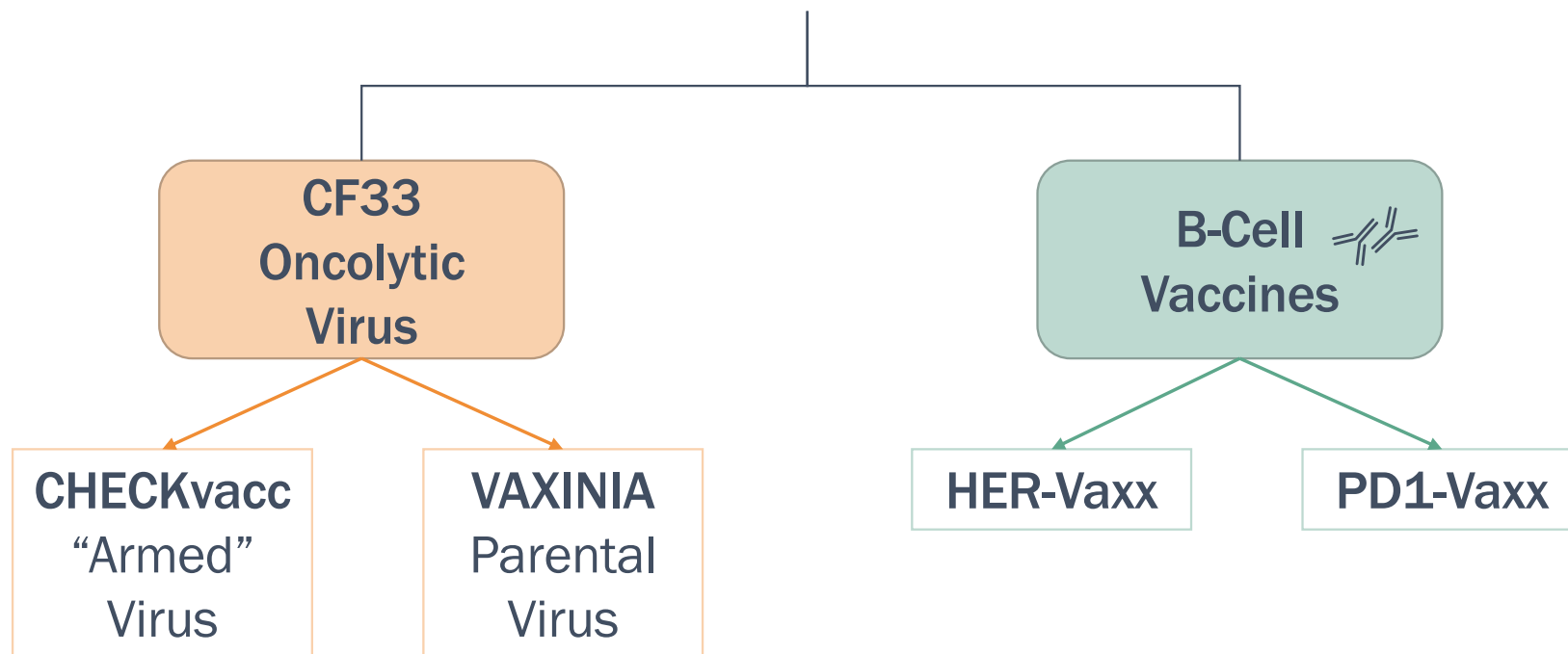
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## INVESTMENT HIGHLIGHTS

- Two novel technologies: B-Cell activating immunotherapies and CF33 oncolytic virotherapy
- B-Cell Technologies: HER-Vaxx Positive Interim Data read out for Phase 2 trial in gastric cancer
- B-Cell Technologies: PD1-Vaxx screening patients in Phase 1 for NSCLC
- CF33 from City of Hope Cancer Centre in Los Angeles
- CF33 has demonstrated single agent & combination activity
- CF33 has prolific and compelling pre-clinical data
- CF33 GMP manufacturing complete for both trials
- Highly experienced CF33 team including CMO from ex OV biotech company and ex-Viralytics clinical development team
- Robust, long life IP portfolio over both technologies
- Significant news flow with multiple near & medium term valuation inflections



# TWO NOVEL TECHNOLOGY PLATFORMS



# IMUGENE'S DEEP PIPELINE



	Pre-Clinical	Clinical development Phase 1	Clinical development Phase 2	Key Data / Results	Intellectual Property
<b>VAXINIA (CF33)</b>		Mixed Advanced solid tumors		<ul style="list-style-type: none"> <li>CF33 has shown strong anti tumour responses in preclinical studies</li> <li>Inhibition of tumour growth in nearly all NCI60 models in TNBC, Lung, Pancreatic etc.</li> <li>Signs of increased tumour growth inhibition with CF33 + anti PD-L1</li> </ul>	Expiring 2037
<b>CHECKvacc (CF33 &amp; aPD-L1)</b>		Triple negative breast cancer		<ul style="list-style-type: none"> <li>Pre-clinical studies showed cancer growth inhibition was better than compared to Amgen or Genelux oncolytic virus.</li> <li>Potentially solves the industry problem of additive toxicity of combined checkpoint inhibitors if safety of CF33 is maintained in combination</li> </ul>	Expiring 2037
<b>HER-Vaxx (HER-2)</b>			Gastric	<ul style="list-style-type: none"> <li>Successful completion of Phase 1b trials, published in AACR, ASCO GI, ASCO, ESMO GI, ESMO, ESMO Asia 2019</li> <li>Strong trial results with no safety or toxicity issues, all patients had increased antibody response, 11/14 evaluable patients with encouraging clinical responses</li> <li>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.</li> </ul>	Expiring 2036
<b>PD1-Vaxx</b>		Lung		<ul style="list-style-type: none"> <li>PD1-Vaxx has shown encouraging response in preclinical studies</li> <li>Strong inhibition of tumour growth in mouse models of colorectal cancer (outperformed industry standard mouse PD-1 mAb)</li> <li>Signs of increased tumour growth inhibition when co-administered with B-Vaxx</li> </ul>	Expiring 2037

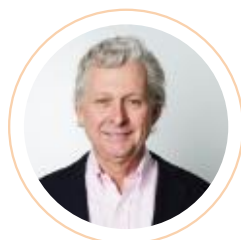
## International Leadership Team with Extensive Commercialization Expertise in the Sector



**Leslie Chong**  
SYDNEY, AU

Managing Director & CEO

- 21+ 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)



**Paul Hopper**  
SYDNEY, AU

Executive Chairman

- Founder of Imugene
- Former Chairman of Viralytics
- Founder & Director of Prescient
- Chairman of SUDA Pharmaceutical
- Extensive international & ASX biotech capital markets experience particularly in immuno-oncology & vaccines
- Co-Chairman of Scopus Biopharma based in New York.



**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

- 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<sup>2</sup> Therapeutics in Boston
- Chairman of the Sabin Vaccine Institute
- Co-Chair of the Cancer Immunotherapy Consortium Think-Tank



**Mr 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

Imugene has a team with oncology drug development experience

# Experienced management team which have significant clinical development expertise



**Dr Rita Laeufle**  
SAN DIEGO, USA  
Chief Medical Officer

- 27+ years of oncology experience in academia and industry
- Clinical development experience with bevacizumab, trastuzumab, abinituzumab, CPIs and oncolytic viruses from Phase I – to post marketing Phase IV
- Former CMO at Oncolytics Biotech, Ex Genentech, Ex Hoffmann-La Roche, and Ex Novartis



**Dr Nick Ede**  
MELBOURNE, AU  
Chief Technology Officer

- 25+ years peptide vaccine and drug development
- Former CEO Adistem and CEO of Mimotopes , VP Chemistry Chiron (now Novartis), Research Fellow CRC Vaccine Technology



**Dr Anthony Good**  
SYDNEY, AU  
VP of Clinical Research

- 20+ years experience in global clinical development
- Integral to the development of significant new medicines including Viagra, Revatio, Lipitor, and Somavert
- Ex Pfizer Global Research and Development, Ex Covance Clinical Services



**Bonnie Nixon**  
SYDNEY, AU  
Project Manager

- 5+ years of oncology experience across Phase I – IV clinical trials
- Ex North America Study Manager at Genentech, Ex Roche Clinical Operations Australia

Imugene has a team with oncology drug development experience



## **B-Cell Immunotherapy**



# B CELL BASED ANTIBODIES HAVE DISTINCT 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, 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

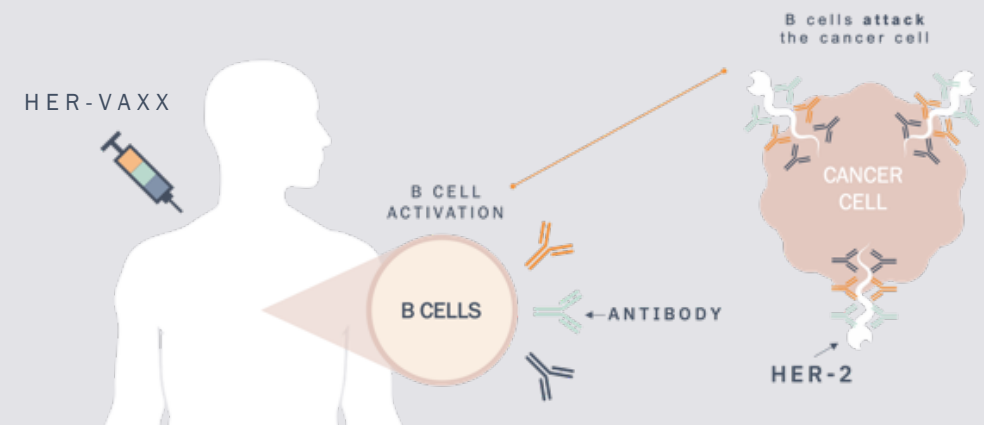
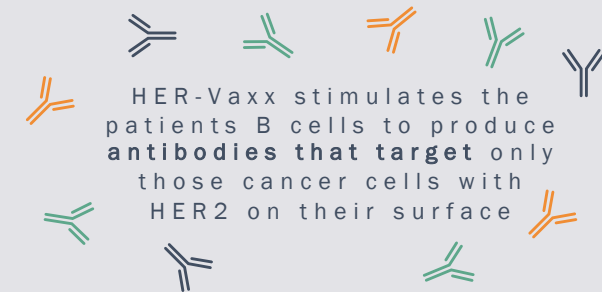
### Cost

Low cost of production enables greater pricing flexibility facilitating combination

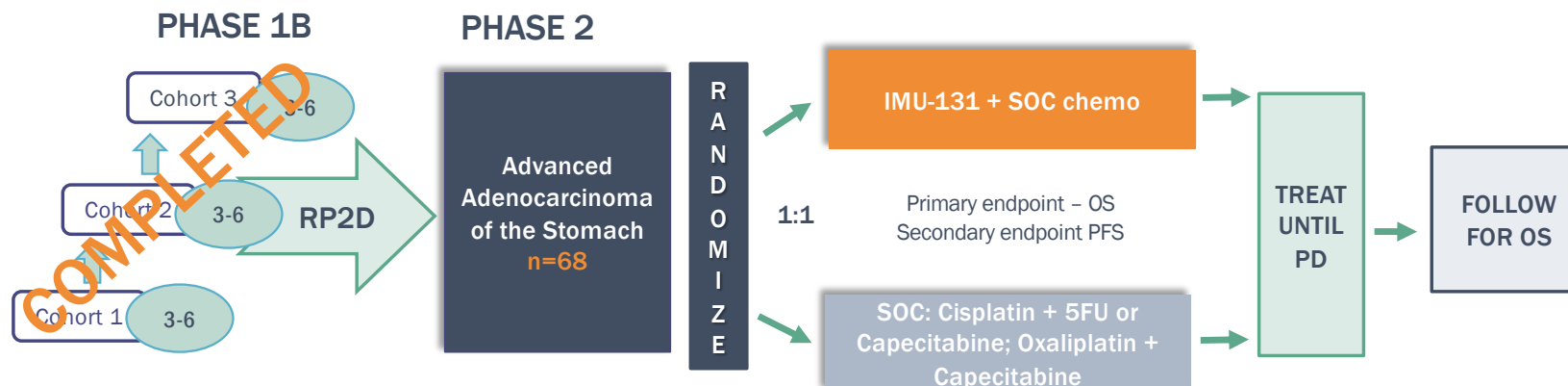
Expensive course of treatment >US\$100K per year

## B-CELL IMMUNOTHERAPY VACCINE AGAINST HER-2

- HER-Vaxx is a **B-cell immunotherapy** designed to treat tumours that over-express the HER2/neu receptor, including **gastric and breast cancer**
- The immunotherapy is **constructed from three B cell epitopes** derived from the extracellular domain of HER2/neu
- HER-Vaxx is **under development for the treatment of HER2-positive gastric cancer**, and also has the potential to treat other HER2-overexpressing cancers
- HER-Vaxx has been shown in pre-clinical studies and now in a Phase I study to stimulate a **potent polyclonal antibody response** to HER2/neu, a well-validated cancer target



# HER-Vaxx PHASE 1B/2 STUDY DESIGN



Phase	Phase 1B	Phase 2
Indication	Newly diagnosed HER2+ gastric cancer	Newly diagnosed HER2+ gastric cancer
Objectives	Safety & Tolerability, Immunogenicity, RP2D	Primary: OS, Secondary: PFS, Safety & Tolerability, Immune Response
No. of Patients	14	68
Site Location	Asia, Eastern Europe, India	Eastern Europe, India

# HER-Vaxx PHASE 1B: DESIGN & RESULTS



## Trial

- HER2 Gastric or GEJ cancer
- Phase 1b
- Open label
- Dose escalation
- 14 sites in Asia and Eastern Europe



## Patients

- Advanced stage IIIb or IV
- 7 HER2+++ , 3 HER2++ (FISH positive), 4 HER2++ expressing tumors
- Age 57yo (21 - 79)
- ECOG 1(7) and 0(7)
- 9 Asian, 5 Caucasian
- 5 female, 9 male



## Study

- 14 patients in 3 cohorts (10µg (3), 30µg (6) and 50µg (5))
- Dosed on D0, D14, D35
- IMU-131 in combination with chemo: cisplatin and 5FU or capecitabine



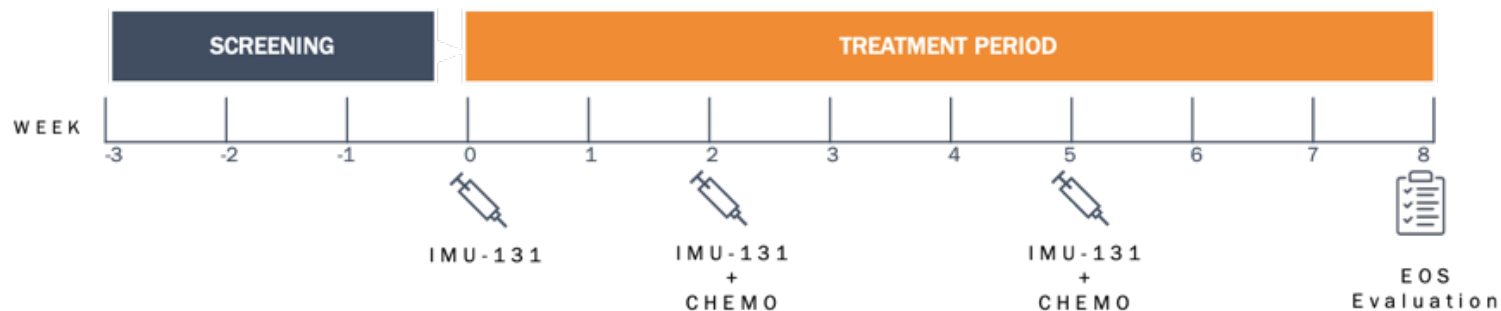
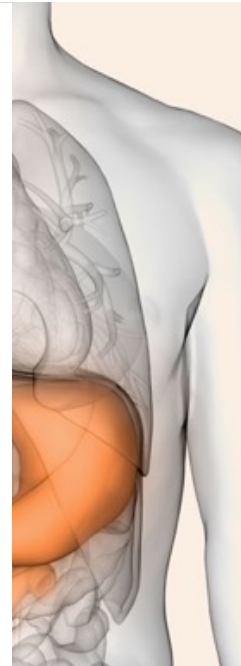
## Endpoints

- Recommended Phase 2 Dose of IMU-131
- Safety and Toxicity
- Immunogenicity (anti-peptide (P467) and anti-HER-2 antibody titres)



## Study Results

- No safety or toxicity issues
- All patients had increased antibody response
- 1 Complete Response
- 5 Partial Response
- 4 Stable Disease
- 1 Progressive Disease
- 50 µg selected as RP2D



# HER-Vaxx PHASE 2: RECRUITING



## Trial

- Phase 2
- Open label
- Eastern Europe
- India



## Patients

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



## Study

### Randomized

HER-Vaxx in combination with standard of care chemotherapy

### Or

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

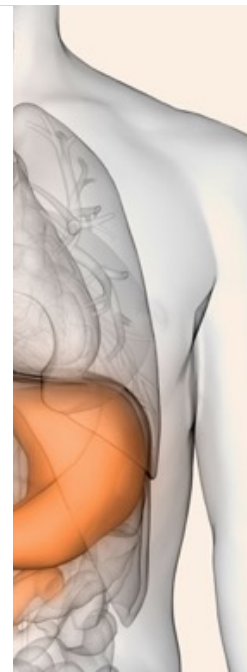


## Primary Endpoints

- Overall survival

## Secondary Endpoints

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



# HER-Vaxx PHASE 2: INTERIM ANALYSIS

## Efficacy Outcome Overview

Endpoint	OS ITT * (Primary)	
	Chemo	Chemo+ HER-Vaxx
All Patients n=27 (at data cut off)	13	14
Events**	8	4
Hazard Ratio (HR)	0.418	
2-sided 80%CI	(0.186,0.942)	
Log-rank Test (1-sided p-value)***	.083 <sup>+</sup>	

\*Overall Survival Intent to Treat

\*\*Death

\*\*\*Pre-specified alpha at 0.10

<sup>+</sup> Statistically Significant

# HER-Vaxx PHASE 2: INTERIM ANALYSIS

## Safety Overview - Patients with at least one TEAE\*

Total at data cut off	Chemo + HER-Vaxx %	Chemo alone %
Grade 3	42.9%	30.8%
Grade 4	0%	15.4%
Grade 5	0%	7.7%

\*Treatment Emergent Adverse Events showed **no added Toxicity to HER-Vaxx and Chemo arm** independent of causality

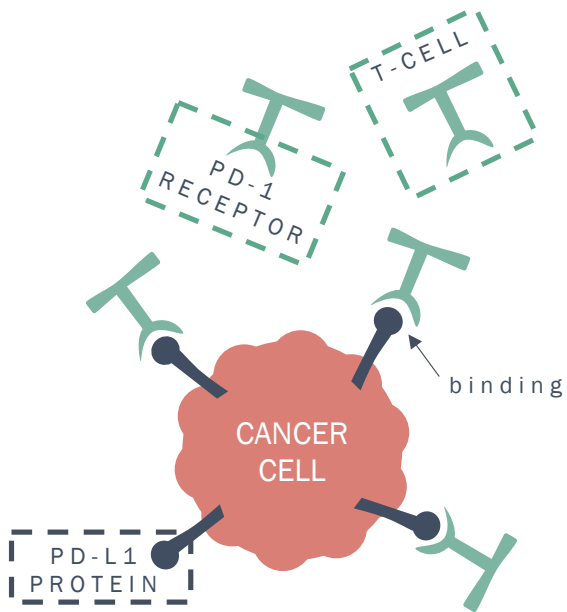
## HER-Vaxx PHASE 2: INTERIM ANALYSIS

- ✓ Interim analysis showed statistically significant overall survival Hazard Ratio (HR) of **0.418** (80% 2-sided CI: 0.186, 0.942); HER-Vaxx showed a reduced risk of death of **58.2%** in the HER-Vaxx plus chemotherapy group as compared to chemotherapy alone.
- ✓ The median overall survival (OS) for patients receiving HER-Vaxx plus chemotherapy was **14.2 months**, compared to **8.8 months** in patients treated with chemotherapy alone.
- ✓ The Independent Data Monitoring Committee (**IDMC**) confirms a favourable survival outcome with no added toxicity for HER-Vaxx combined with SOC chemotherapy over chemotherapy alone and advised to **reduce the overall number of patients to ~34** and number of required events **given the strong signal** that it would be considered unethical to enroll 68 as originally planned.
- ✓ The IDMC agreed, that the safety of the study is favorable with **no added toxicity** for the combination of HER-Vaxx and SOC chemotherapy versus SOC chemotherapy alone.
- ✓ The IDMC agreed that the presented data is strongly encouraging to conclude that the combination of **HER-Vaxx and SOC Chemotherapy is safe**.
- ✓ The Phase 2 data represent a **clinical proof-of-concept signal for HER-Vaxx** when added to chemotherapy and indicate that B-cell activating immunotherapy vaccines can induce clinically active antibody responses.



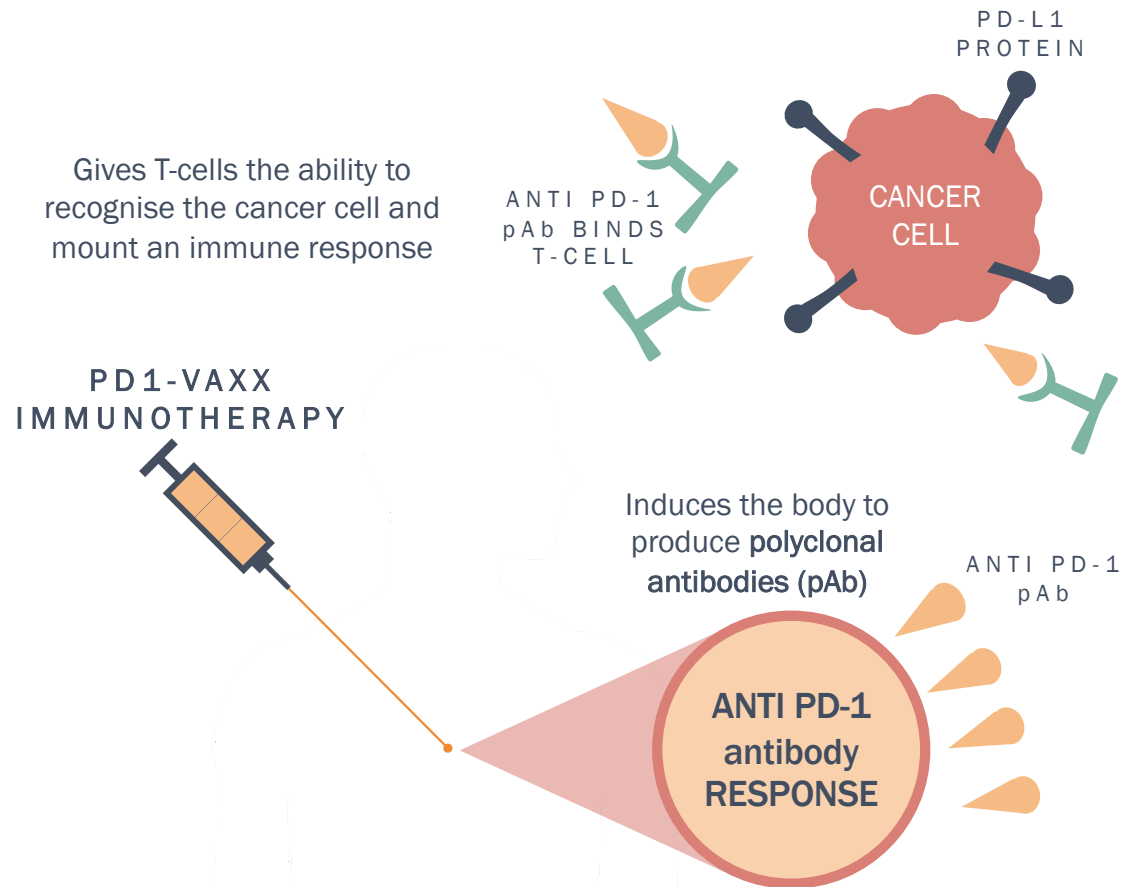
# HOW DOES PD1-Vaxx WORK?

## HOW CANCER STAYS UNDETECTED BY THE IMMUNE SYSTEM



The PD-L1 protein binds to the PD-1 receptor and stops the T-Cell from recognising the cancer cell, allowing the cancer cell to survive and spread

## PD1-VAXX STOPS THE CANCER CELL FROM AVOIDING T-CELL RECOGNITION AND KILLING

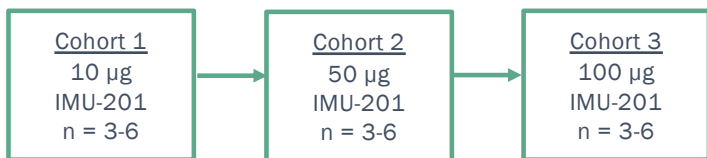


# PD1-Vaxx PHASE 1: STUDY DESIGN

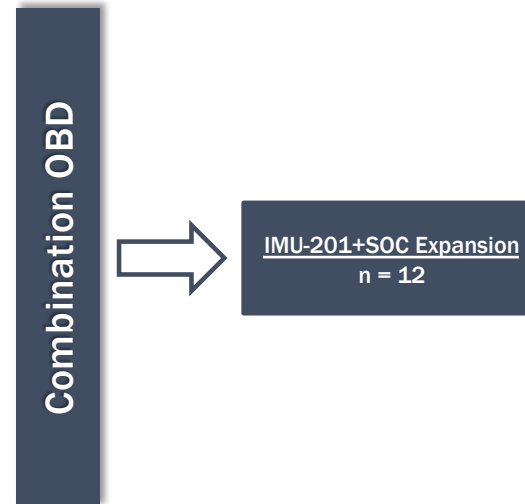
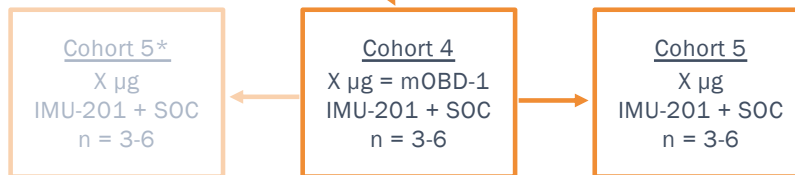
## Part 1: Monotherapy Dose Escalation

## Part 2: Combination Escalation & Dose Expansion (Planned)

### PD1-Vaxx Monotherapy (MTD/OBD evaluation)



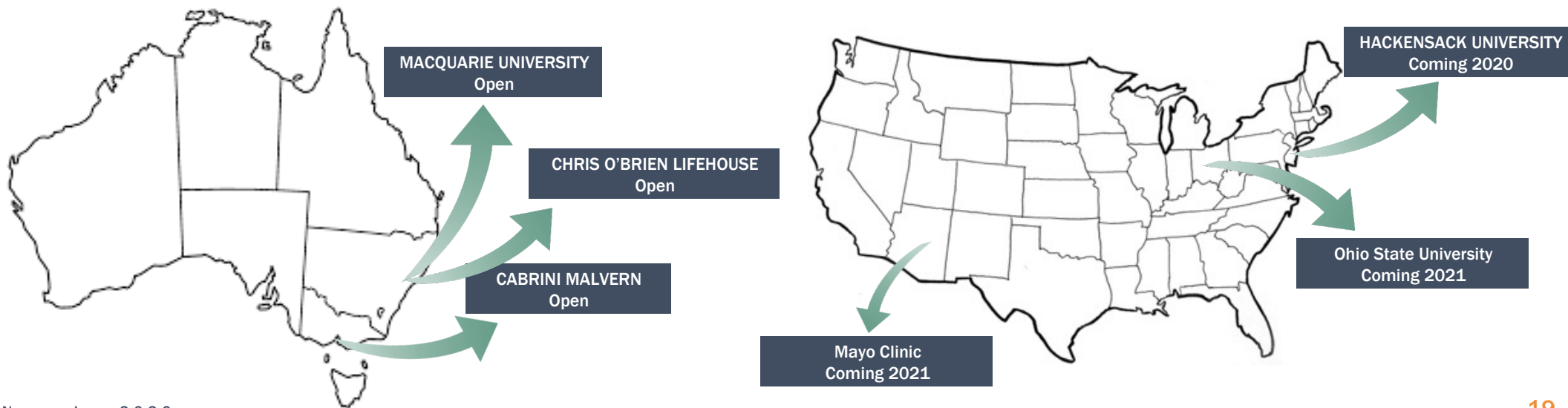
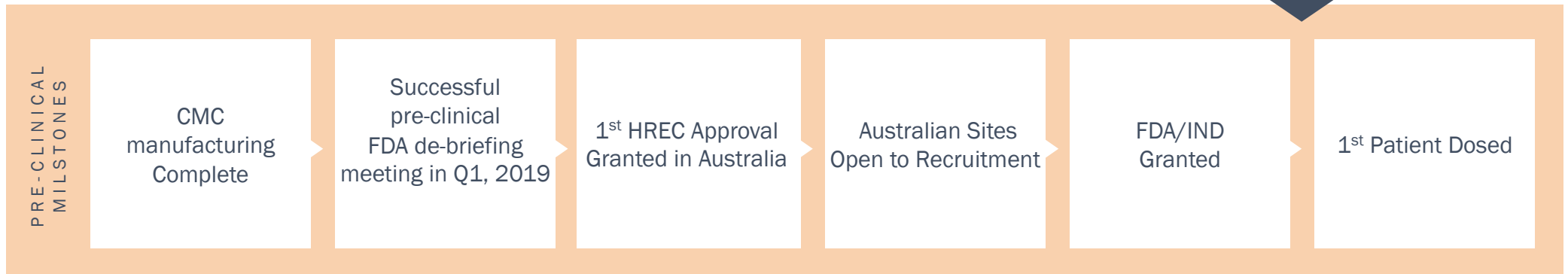
### PD1-Vaxx + SOC Combination (MTD/OBD evaluation)



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

Current status

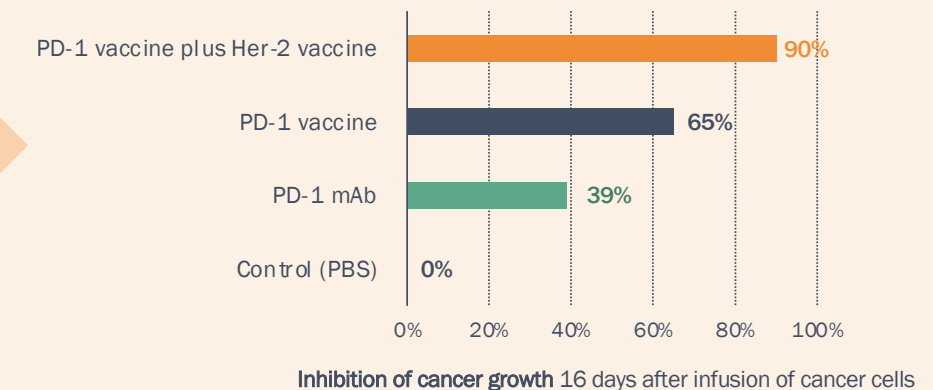


# PD-1/HER-2 COMBINATION: POTENTIAL TO INCREASE RESPONSE RATES IN HER-2+ CANCERS

## Immuno-oncology combinations are driving value

- Combining drugs for **better immuno-oncology outcome** is driving value creation
- Big Pharma are looking for **novel combinations** that
  - ✓ Combine without increasing toxicity
  - ✓ Combine with minimal cost increase
  - ✓ Combine for better response rates and efficacy

% CANCER GROWTH INHIBITION IN COLORECTAL CANCER MODEL



Imugene's novel therapies have the potential to tick all three boxes

## Opdivo / Yervoy Case Study

In 2018, the FDA approved the Opdivo and Yervoy combination for a subset of patients with metastatic colorectal cancer

Provides a novel therapeutic option with a higher response rate than that from monotherapy immunotherapy

**BUT** more significant toxicity is noted with the combination, and immune-mediated side effects need to be monitored

Although early in development, Imugene's PD-1 and Her-2 cancer vaccines potentially provide efficacy and response rate with minimal toxicity

# IMUGENE'S DISCOVERY PIPELINE

Imugene has the ability to advance these programs at any point

## Program

## Pre-clinical

## ID of candidate

Her-1 (EGFR)

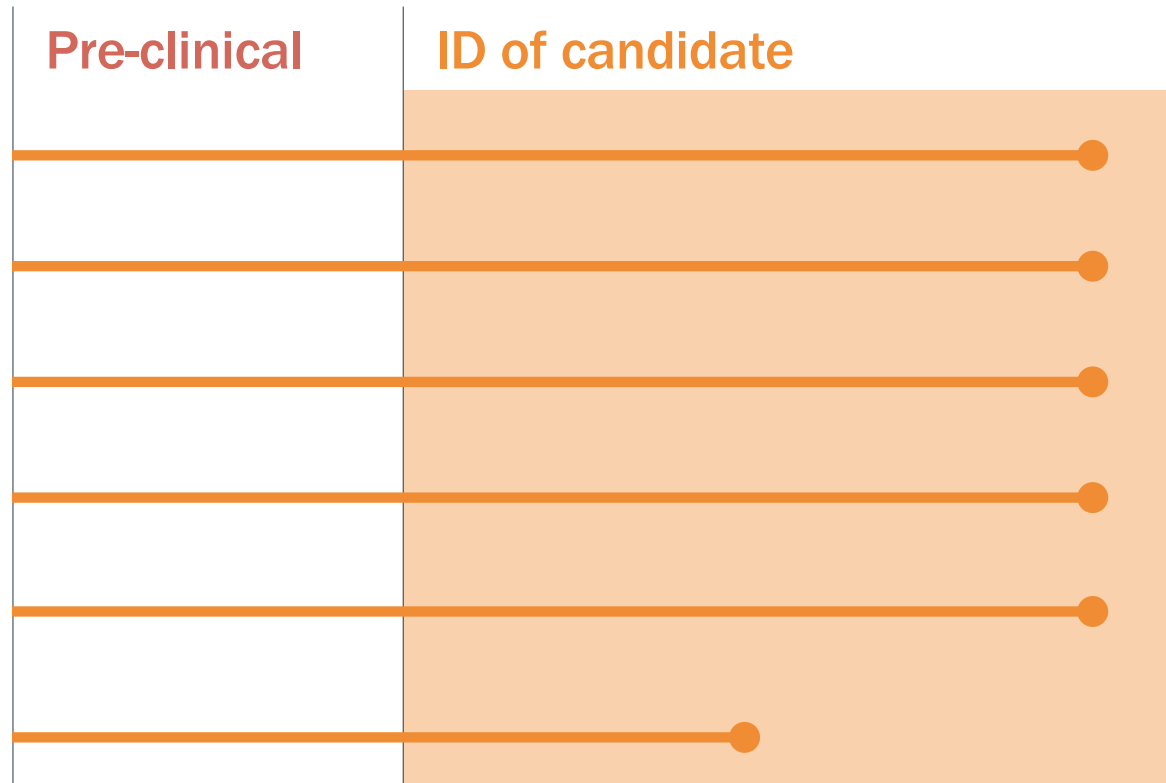
Her-3

IGF-1R

VEGF

PD-L1

Combination  
(numerous)

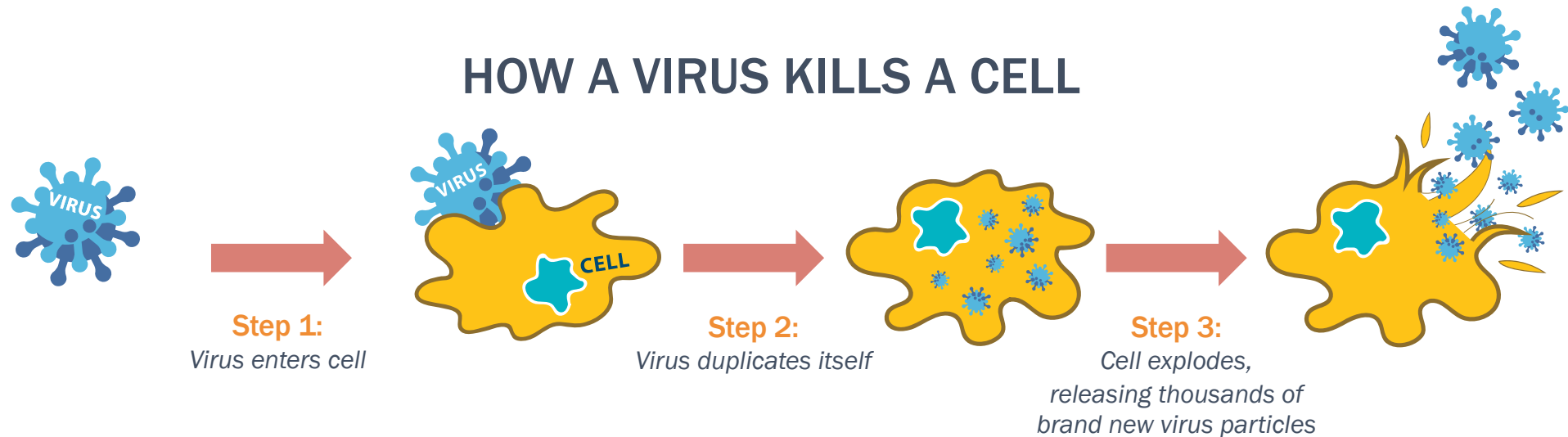




## **CF33: Oncolytic Virus**

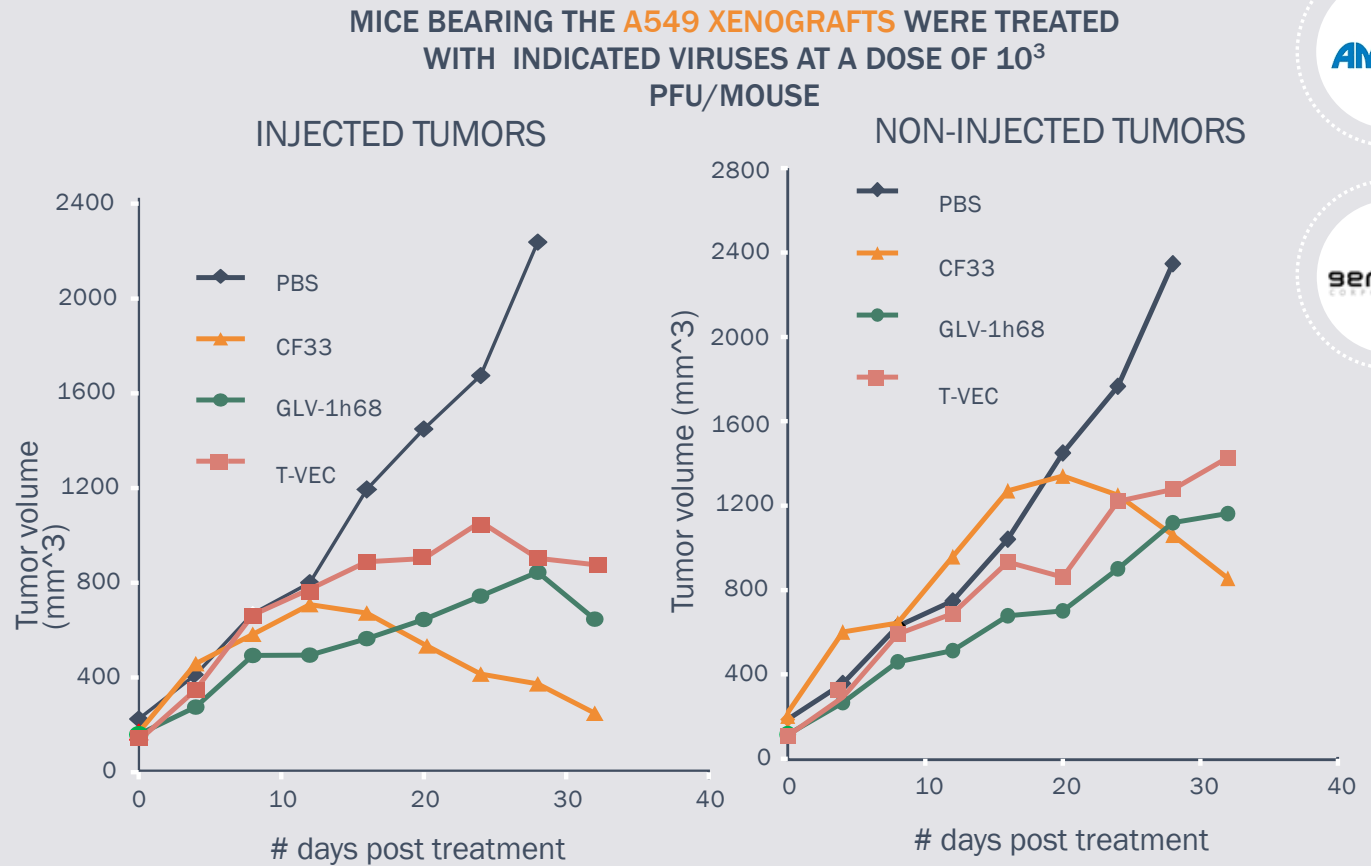
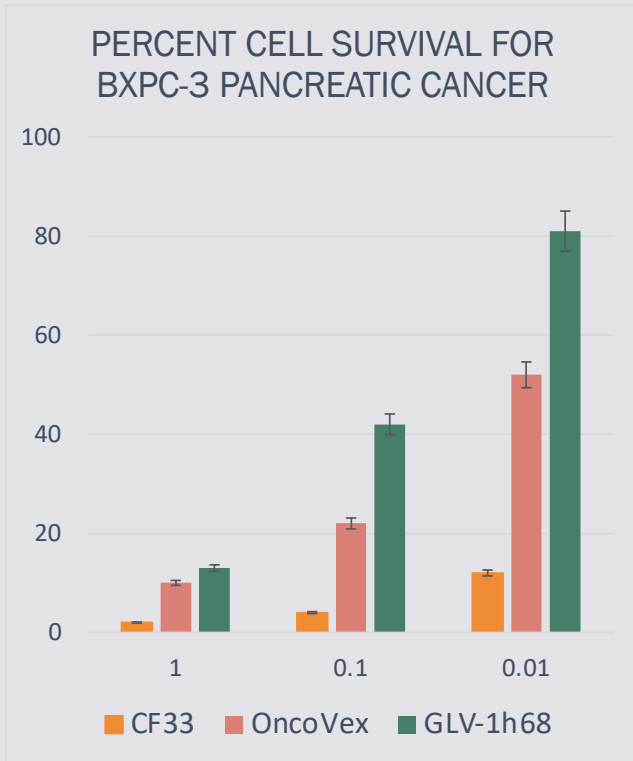
# CF33 MECHANISM OF ACTION

## HOW A VIRUS KILLS A CELL



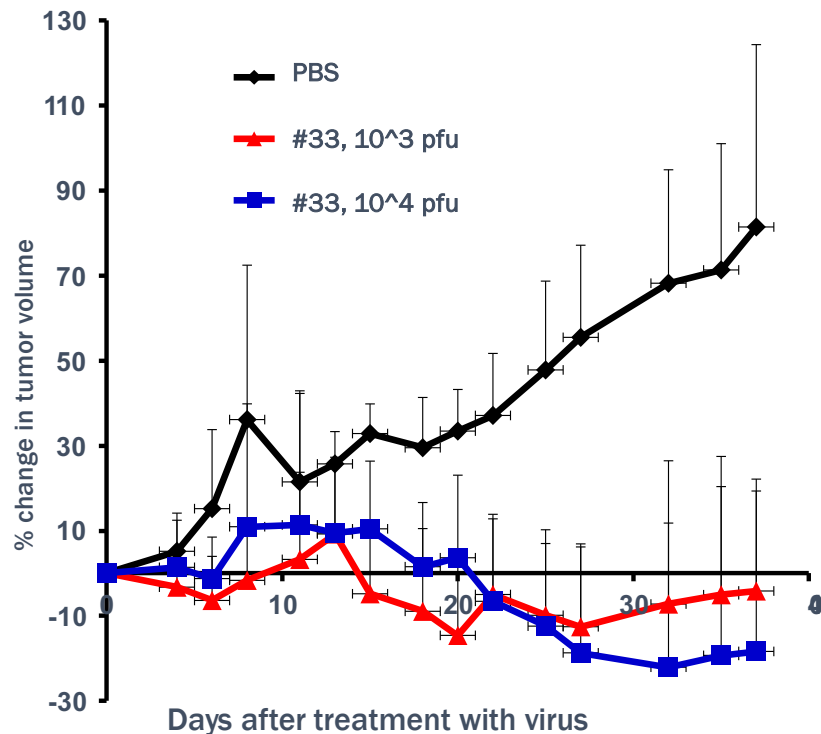
- Direct infection, replication within and cancer cell killing
- Viral infection increases local check point targets (PD-1, PD-L1, CTLA4 etc)
- Cell death is immunogenic [surface expression of calreticulin, release of adenosine triphosphate (ATP) and release of high mobility group box 1 (HMGB1)]
- Local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

# CF33 OUTPERFORMS AMGEN & GENELUX VIRUSES





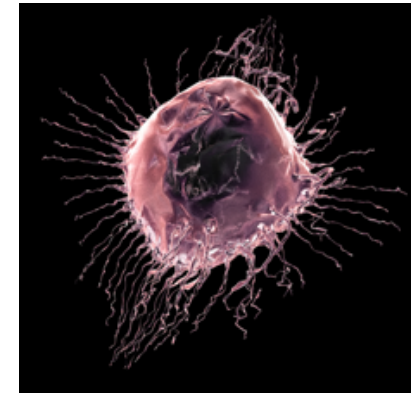
# CF33 SHRINKS TRIPLE-NEGATIVE BREAST CANCER



*Mice treated with both intratumoral virus and IV*

The viral dose used was **2-5 orders of magnitude** lower than doses used for oncolytic viruses under clinical testing

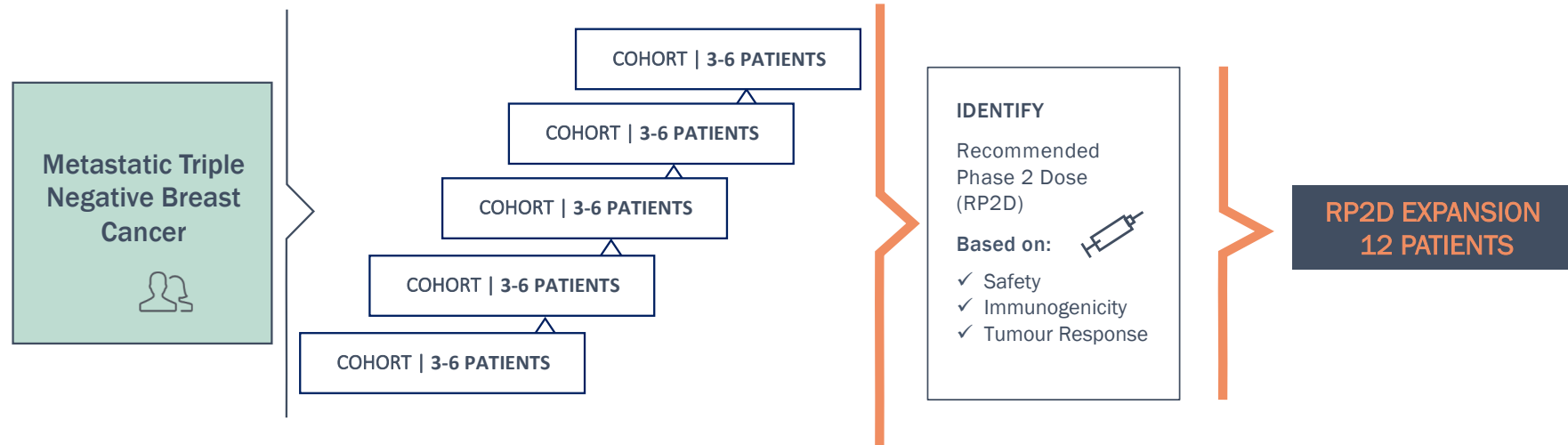
*Mol Ther Oncolytics.  
2018 Jun 29;9*






The viral dose used was **2-5 orders of magnitude** lower than doses used for oncolytic viruses under clinical testing

# CHECKvacc: CF33+hNIS+aPD-L1 (“Armed” Virus)

## Phase 1 Triple Negative Breast Cancer Study – GMP Manufacturing Complete



- ❑ 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)
  - 1<sup>st</sup> line: 24%; 2<sup>nd</sup> line: 6%
  - Approved by FDA 8-March, 2019
- ❑ Potential for registration in well-designed, randomized P2 study

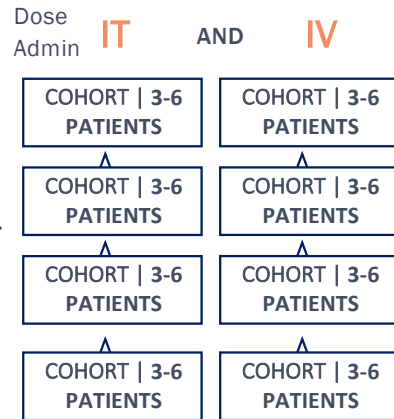
	<b>Indication</b>	TNBC
	<b>FDA IND</b>	CHECKvacc: CF33-hNIS-aPDL1
	<b>N</b>	Part 1=18-24 ; Part 2=12
	<b>Location</b>	Single Center: COH
	<b>Admin Route</b>	Intratumoral (IT)

# VAXINIA PHASE 1 MAST STUDY (Metastatic Advanced Solid Tumours)

## Part 1: VAXINIA Monotherapy Dose Escalation

**IT Administration**  
Head & Neck,  
Advanced  
Melanoma, TNBC

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




**IDENTIFY MONOTHERAPY**

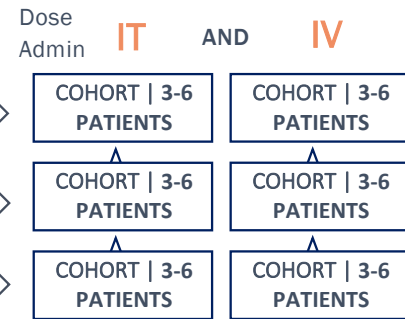
Maximum Feasible Does (MFD)

**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 PD and target Signals

<b>Phase</b>	Phase 1	
<b>Indication</b>		IT: Head & Neck, Advanced Melanoma, TNBC IV: Head & Neck, Advanced Melanoma, TNBC, NSCLC, Bladder, Gastric, Colorectal, RCC
<b>Objectives</b>		Safety & MFD
<b>No. of Patients</b>		Approx. 60-120
<b>Site Location</b>		USA

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

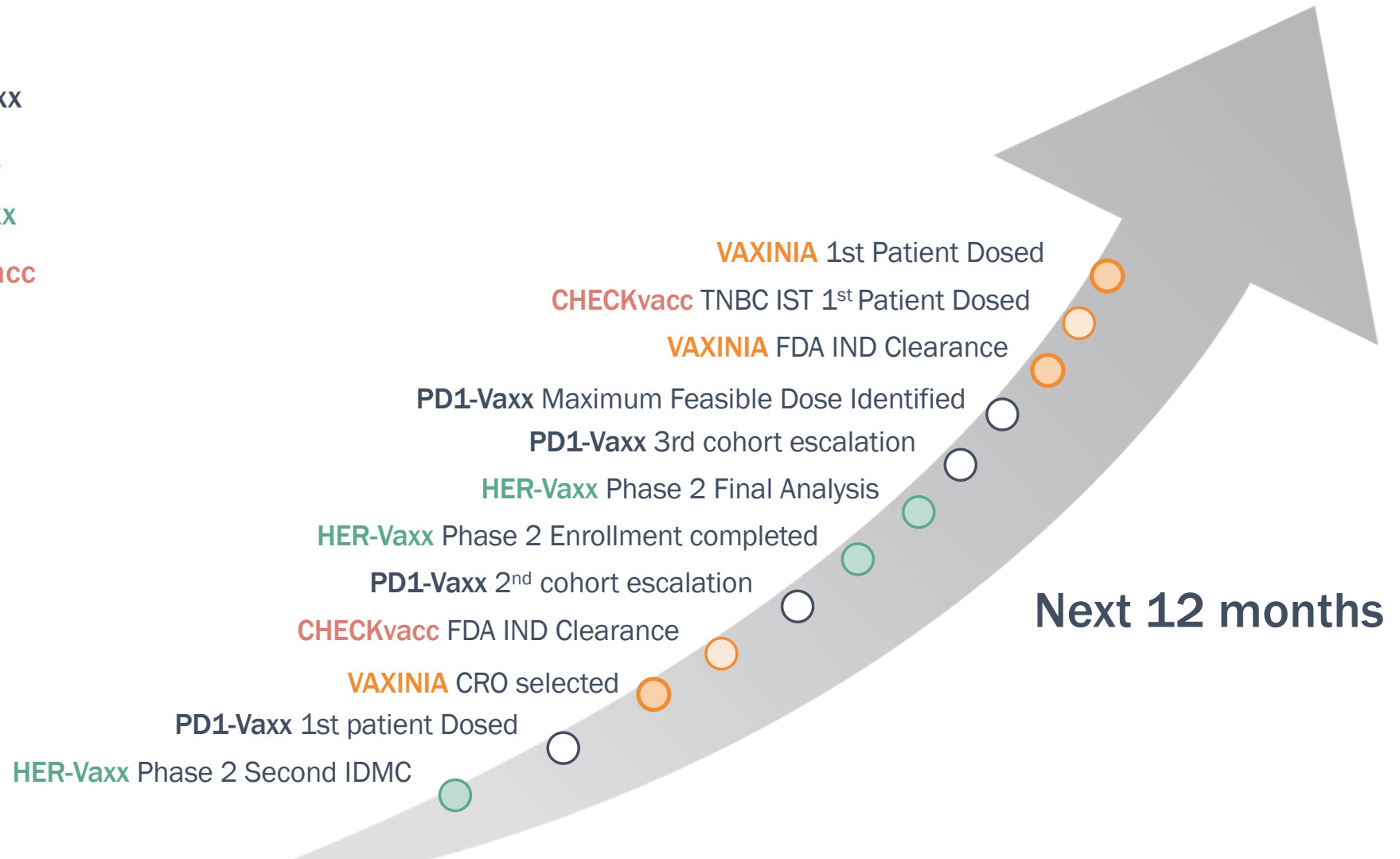
# LANDSCAPE: RECENT ONCOLYTIC VIRUS TRANSACTIONS

Date	January 2011	February 2018	May 2018	September 2018	December 2019
<b>Oncolytic Virus Company</b>					
<b>Focused virus technology</b>	Onco-vex (herpes)	Coxsackie virus A21	Herpes virus	VSV (vesicular stomatitis virus)	Vaccinia Virus
<b>Partnership Company</b>			   		
<b>Phase of Development</b>	Approved 2015  (talimogene laherparepvec)	<b>Phase 1</b>	<b>Pre-clinical</b>	<b>Pre-clinical</b>	<b>Pre-clinical</b>
<b>Upfront</b>	\$425 million	\$394 million	\$140 million	\$245 million	\$120 million
<b>Potential milestones</b>	\$575 million	-	\$900 million	-	\$900 million
<b>Total Deal Value</b>	<b>\$1 billion</b>	<b>\$394 million</b>	<b>\$1.04 billion</b>	<b>\$245 million</b>	<b>\$1.2 billion</b>

~\$3.7 billion USD in total value) with 3 Deals Done in Preclinical Stage

# MULTIPLE NEAR & MEDIUM TERM VALUE INFLECTION POINTS

- PD1-Vaxx
- VAXINIA
- HER-Vaxx
- CHECKvacc



# FINANCIAL SUMMARY



## Public Market Overview

Share Price <sup>1</sup>	A\$0.115
Market Capitalisation <sup>2</sup>	A\$528.4M
Cash equivalents (30 Sep 20)	A\$26.6M
Enterprise Value	A\$501.8M

## Top 5 Shareholders (as at November 2020)

Richard Mann and Assoc.	5.66%
Paul Hopper	3.86%
National Nominees Limited	2.77%
Dr Nicholas Smith	2.57%
HSBC Custody Nominees (Australia)	1.82%

Note:

1. As of 23 November 2020
2. Market capitalization calculations based on ordinary shares (4.59bn) only and excludes the dilutive impact of options outstanding (842m)

## Share Price Performance (last 6 months)





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