

## Corporate Presentation Q4, 2015

Leslie Chong – Chief Operating Officer



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# Investment Highlights



## Leadership

- Experienced management & board – Board & management own 13%

## Compelling Science

- B-cell peptide cancer immunotherapy that induces antibody responses + major new initiative into mimotopes

## Commercially Validated Target

- Targeting same receptor as Roche's \$6.4bn breast cancer drug Herceptin

## Phase 1 Completed

- Anti- HER-2 antibody responses, T helper cytokines, T reg cells suppressed, therapy safe

## Robust IP

- IP with exclusivity until 2030, granted in all major jurisdictions. Further patent life extensions under way

## News Flow

- Numerous milestone announcements & valuation inflection points over next 12-24 months



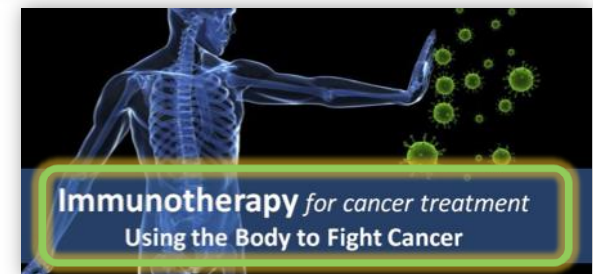
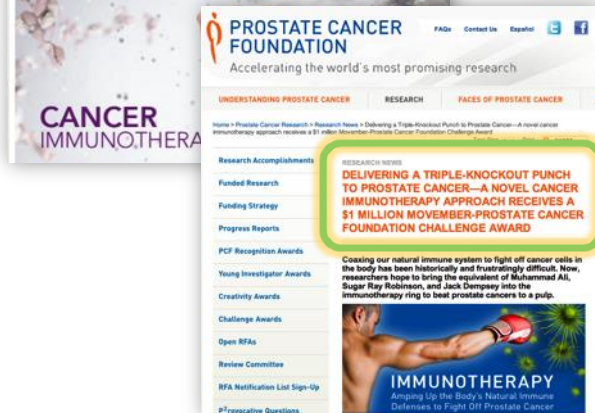
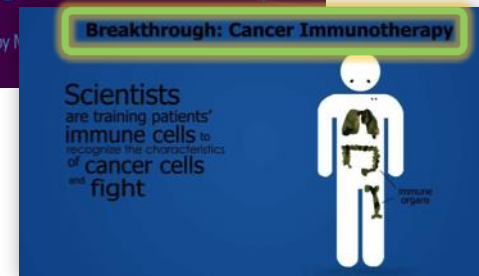
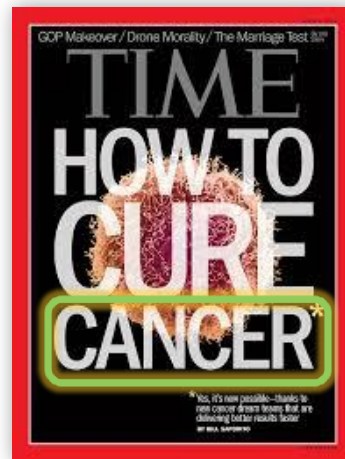
## **Developing B-cell based immunotherapy vaccines plus major new initiative into mimotopes**

- Phase 1 trial completed in patients with HER-2+/++ breast cancer
- Phase 1b/2 gastric cancer trial to begin early 2016
- Technology originates from Medical University of Vienna, one of Europe's leading cancer institutes
- Technology identified in 2012 by Axel Hoos and referred to Paul Hopper
- Manufacturing, clinical and regulatory initiatives began in 2013
- Public listing on ASX in December 2013 via reverse merger into listed shell, Imugene Ltd - Axel Hoos joins the Board – his only Board worldwide
- 2014 – manufacturing, clinical & regulatory development continues
- 2015 – Leslie Chong (ex Genentech) appointed COO
- \$9M raised to date



# IMU is in the Most Promising Area of Oncology Today

Imugene is an immunotherapy company developing B-cell based vaccines in the most promising area of oncology today – IMMUNO-ONCOLOGY



# Leadership – Extensive Drug Development Experience



**Leslie Chong** – *Chief Operating Officer*

- Appointment as COO in August 2015
- Previously Senior Clinical Program Lead at Genentech, Inc., in San Francisco



**Prof Ursula Wiedermann** – *Chief Scientific Officer*

- Co-inventor of technology
- Prof of Vaccinology at Medical University of Vienna



**Dr Axel Hoos** – *Non-Executive Director*

- Currently Vice President Oncology R&D at GlaxoSmithKline
- Previously Clinical Lead on Ipilumimab at Bristol-Myers Squibb
- Co-Director of the think-tank Cancer Immunotherapy Consortium; **Imugene is his only Board seat worldwide**



**Dr Nick Ede** – *Head of Manufacturing*

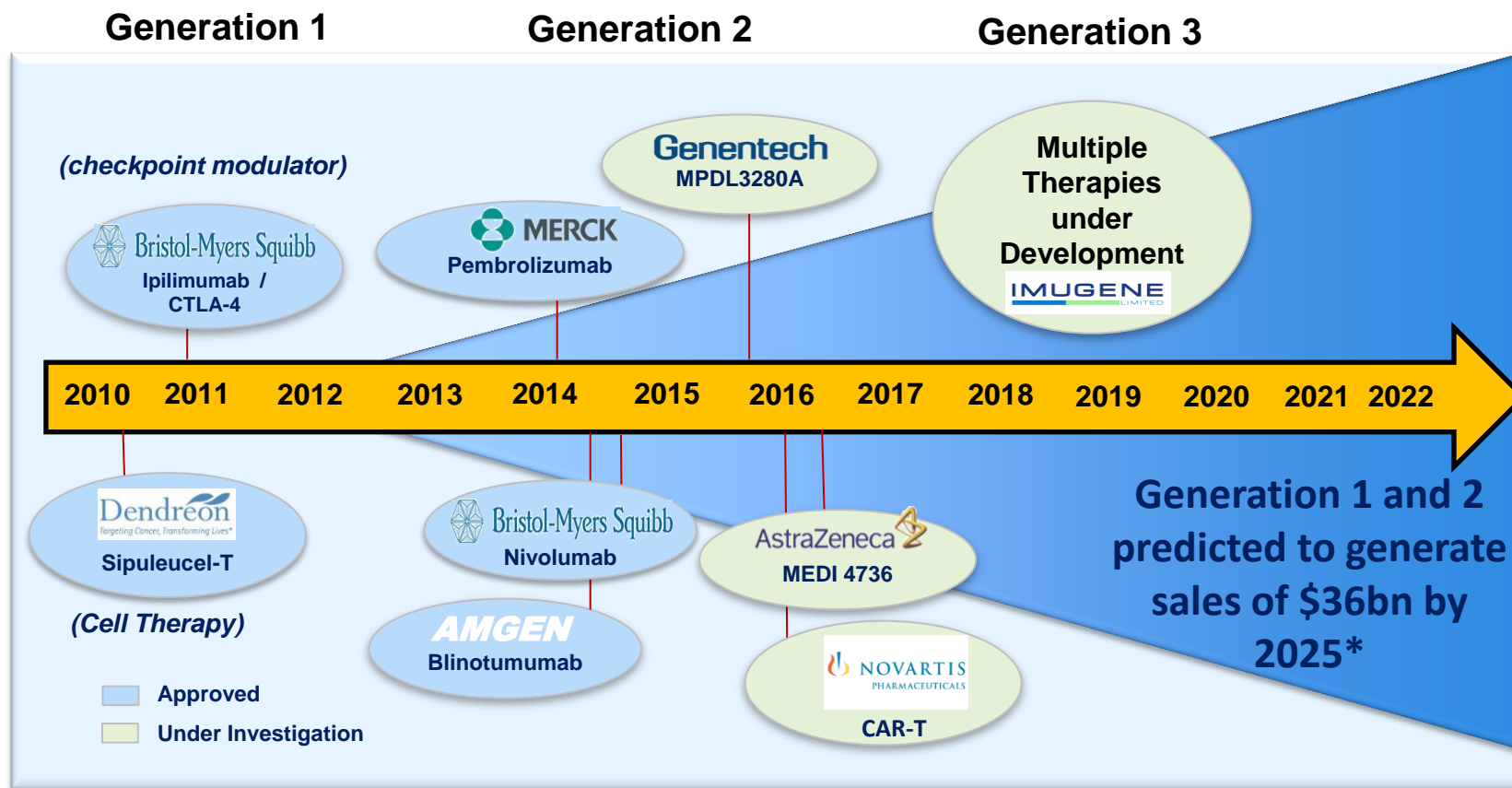
- Former CTO Consegna, CEO Adistem Ltd, CEO Mimotopes P/L, COO EQiTX Ltd (ZingoTX & VacTX)
- VP Chemistry Chiron (now Novartis), Research Fellow CRC Vaccine Technology



**Paul Hopper** – *Executive Chairman*

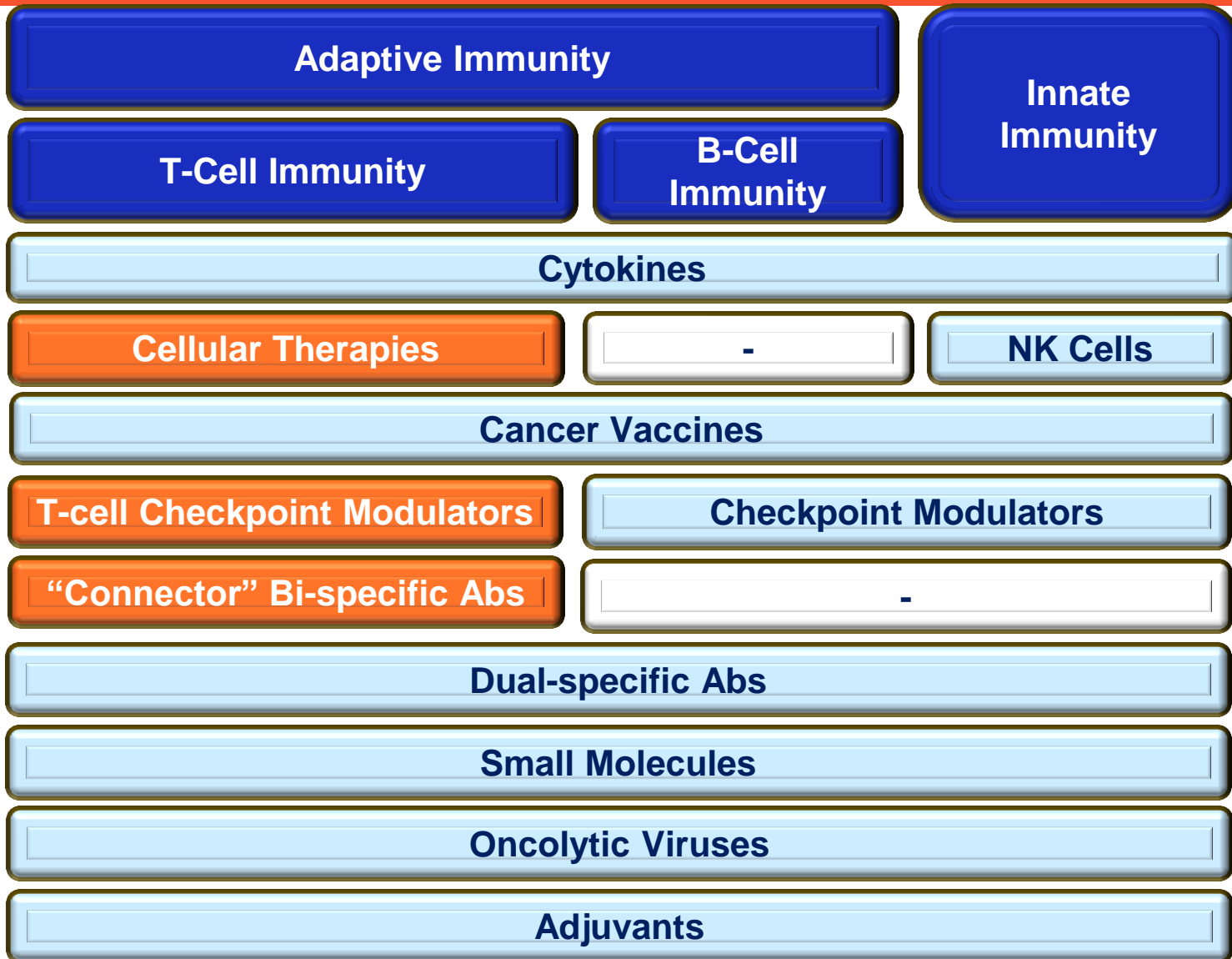
- International & ASX biotech capital markets experience particularly in immuno-oncology & vaccines
- Head of Life Sciences Desk & Australia Desk at Los Angeles-based investment bank, Cappello Group
- Director Prescient Therapeutics, Chairman Viralytics, former Director pSivida, Somnomed & Fibrocell Science

# Immuno-Oncology State of Play



\*Citigroup research note

# Next Wave Opportunities





# Why B-Cell Peptide Vaccines?



- High chemical stability
- Easy construction and manufacturing

- No oncogenic potential
- Immunogenic – break of tumour tolerance

Long-Lasting Immunity

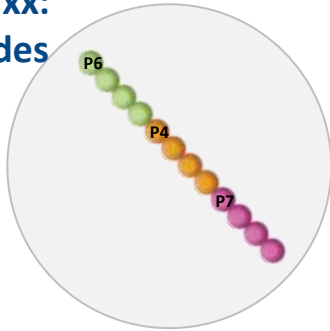
B-Cell Vaccines Offer



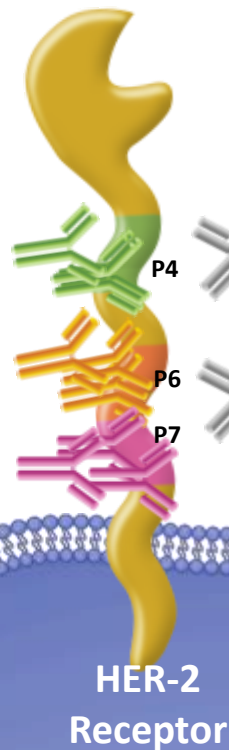
- Anti-tumor activity of antibodies induced by B-cell epitopes
- Patient produces their own antibodies against the target
- Polyclonal responses (superior to treatment with monoclonal antibodies)
- **No HLA restriction!** (advantage over T-cell peptide vaccines)
- Induction of T-cell responses and cytokine production via effective carrier system
- Broader activation of humoral and cellular immune response
- Potential cross-presentation to CD8 T-cells
- Immune memory and potential use of booster vaccinations

# HER-Vaxx Attacks the Same Cancer Receptor the World's Largest Cancer Franchise

HER-Vaxx:  
3 peptides



HER-Vaxx: x3  
polyclonal  
responses



Tumor cell

Binding site of



Binding site of



Monoclonal  
response

Franchise sales annualising at  
nearly \$8bn growing 13%\*




# HER-Vaxx Key Differentiation



- B-cell vaccines are an open frontier for immunotherapy, unlike T cell vaccines which have been exhaustively researched
- HER-Vaxx is a universal vaccine & can be used for all patient types irrespective of their “HLA haplotypes”, an issue which impacts T cell vaccines
- HER-Vaxx generates polyclonal responses that may be superior to treatment with a monoclonal antibody like Herceptin
- Toxicity of HER-Vaxx is negligible
- HER-Vaxx induces IFN $\gamma$  production that can influence the tumour micro environment and suppresses T Reg cells which are enhanced in cancer patients & which assist tumor evasion mechanisms – thereby the efficacy of the HER-Vaxx might be enhanced
- Potential as an adjuvant therapy i.e., post surgery
- **HER-Vaxx is active immunisation** and induces immunological memory – **Herceptin is passive immunisation**, and its effectiveness depends upon frequent applications

# Clinical Status:

## Phase 1 Breast Trial Completed



**Design**

- n=10
- All metastatic breast cancer patients
- HER-2 +/-
- Life expectancy > 4 months
- Conducted at Medical University of Vienna

**Clinical Endpoints**

- 1 Safety and Tolerability
- 2 **Immunogenicity:** antibodies/humoral and cellular responses



# Clinical Status: Phase 1 Breast Trial Completed



Wiedermann et al.,  
*Breast Cancer Res Treat*  
(2010)**119**:673 - 683



## Results

- Patients developed anti-HER-2 antibodies
- Induction of cytokines (Th1 biased; IFN $\gamma$ )
- Induction of memory T & B cells post vaccination
- Reduction in T reg cells post vaccination, indicating strong vaccine response
- Antibodies induced displayed potent anti-tumor activity
- Results were even more promising given patients were in the end stage of disease and not the primary target group



# Phase 1b/2 Trial Design Gastric Cancer



## Combined Phase 1b/2 clinical trial under IND



### Phase 1b lead-in

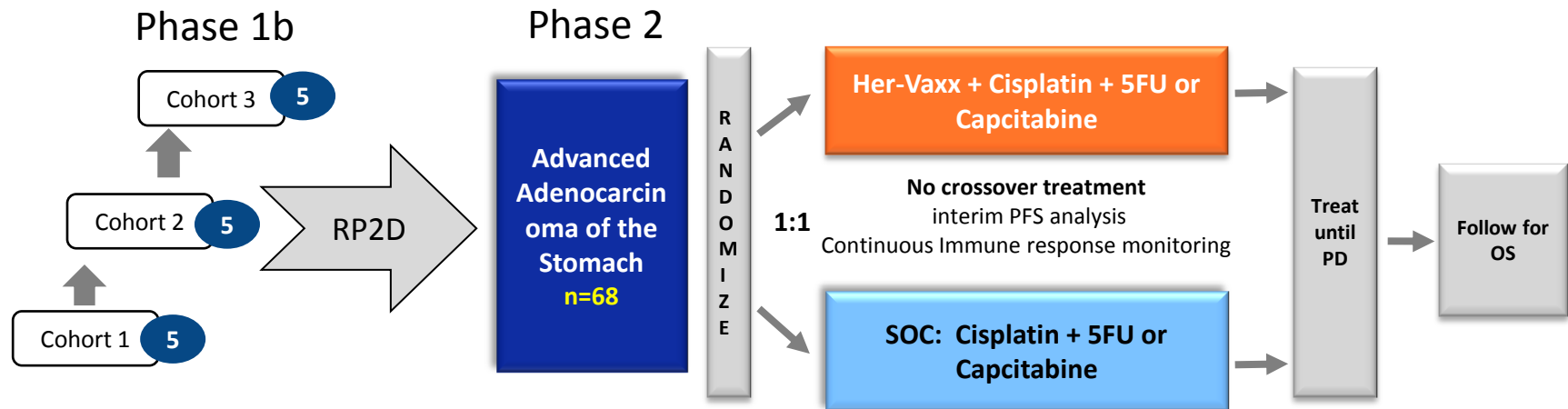
- Open label
- US IND
- 15 patients, x3 groups of 5 patients
- Combination with chemo
- Endpoints:
  - RP2D (Recommended Phase 2 Dose) of HER-Vaxx
  - Safety: any HER-Vaxx toxicity
  - Immunogenicity (anti-HER-2 antibody titers)
  - Test booster schedule (q 4 weeks or 8 weeks)

### Phase 2 Trial

- Open label
- Randomised
- ~68 patients in Asia (2 arms by 34)
- Combination with chemo
- Efficacy, safety & immune response
- Endpoints:
  - Overall survival
  - Progression-free survival
- Secondary endpoint:
  - Immune response



# Phase 1b/2 Trial Design Gastric Cancer



Design	Phase 1b/2
IND Submission	Q1, 2016
Final Protocol	Q1, 2016
N	Phase 1b = 15; Phase II = 68
# Sites	18-20
Enrollment Duration	36 months: Phase 1b = 12 months; Phase 2 = 24 months
FPI	Q2, 2016
End Points	PFS, OS and Immune response
Vendors	IRF, Central Lab

\* under delayed treatment effect on PFS at month 3  
 \*\* OBF for error spending



# Novel Mimotope Technology Platform

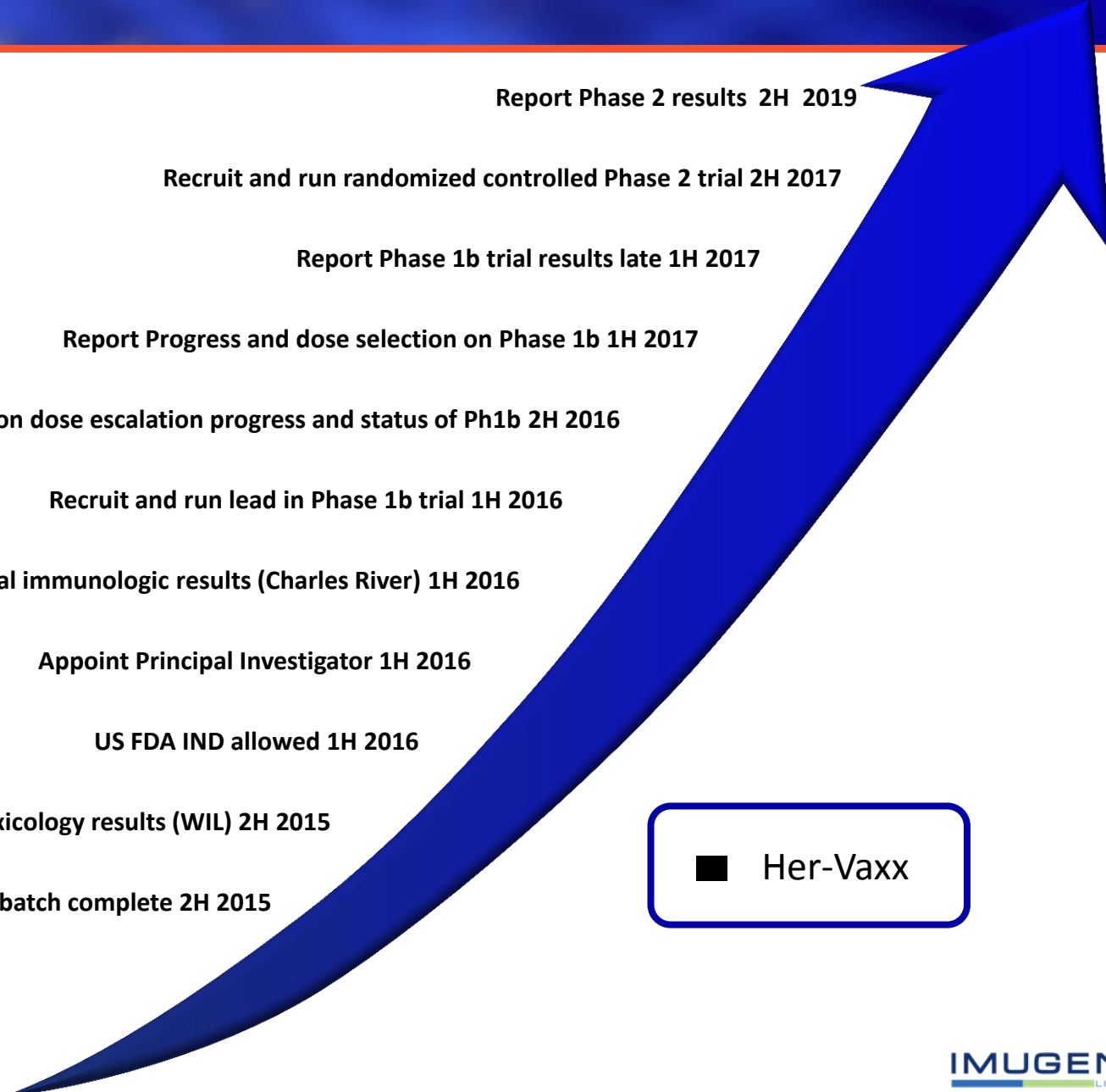


**Imugene's novel mimotope technology platform enables us to reverse engineer any antibody and produce a peptide mimic of the antibody's target (epitope)**

- Developing mimotope immuno-oncology platform against cutting edge immuno-oncology targets, in partnership with Medical University of Vienna
- Mimotopes are peptide antigens which mirror the structure of an epitope and which are designed to induce a specific and potent antibody response to an identified oncology target
- Mimotopes to be part of the next wave of the immuno-oncology revolution
- Potential tool for selecting novel vaccine candidates against a variety of tumours
- Greatly extends the company's oncology franchise and pipeline.
- Four mimotopes to be complete by May 2016 (targets currently confidential)



# News Flow & Milestones



Report Phase 2 results 2H 2019

Recruit and run randomized controlled Phase 2 trial 2H 2017

Report Phase 1b trial results late 1H 2017

Report Progress and dose selection on Phase 1b 1H 2017

Report on dose escalation progress and status of Ph1b 2H 2016

Recruit and run lead in Phase 1b trial 1H 2016

Announce preclinical immunologic results (Charles River) 1H 2016

Appoint Principal Investigator 1H 2016

US FDA IND allowed 1H 2016

Announce preclinical toxicology results (WIL) 2H 2015

Her-Vaxx GMP clinical batch complete 2H 2015

■ Her-Vaxx

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# Appendix

# Capital Structure



## ASX:IMU

Market Cap (Sept 2015)	\$17.0M (AUD) <sup>1</sup>
Ordinary Shares	1,329,912,516B
12 month price range	\$0.01 - \$0.02
Avg daily volume	1.4M shares (June-Sept, 2015)
Public Equity Invested to date	\$9.00M
Cash & Equivalents	\$4.96M (includes Sept 3.0M raise)

## Options on issue (as at 2015)

	No of options	Exercise Price	Expiry
IMUAK	50,000,000	\$0.020	31-Dec-15
IMUAL	2,500,000	\$0.025	14-July-19
IMUAM	4,500,000	\$0.010	10-Nov-17
Total Options on Issue	57,000,000 <sup>2</sup>		

## Top 5 Holders as at 2015

	No. of Shares	% Capital
Webinvest Pty Ltd (Otto Buttula)	77,000,000	5.79
Paul Hopper	69,796,875	5.25
JK Nominees Pty Ltd	40,000,000	3.01
Oaktone Nominees Pty Ltd	29,625,000	2.23
Cabletime Pty Ltd	29,527,778	2.22

## Board and Management Ownership

Otto Buttula	77,000,000	Shares
Paul Hopper	69,000,000	Shares
Axel Hoos	25,000,000 7,000,000	Options Shares
Leslie Chong	25,000,000 2,000,000	Options Shares
Charlie Walker	25,000,000	Shares
Nick Ede	4,500,000 8,000,000	Options Shares

NOTE: 1 inc September 2015 Capital Raise.



# Phase I – Study Design



## Patient inclusion criteria

- Metastatic breast cancer
- HER2 +, ++
- ER/PgR pos.

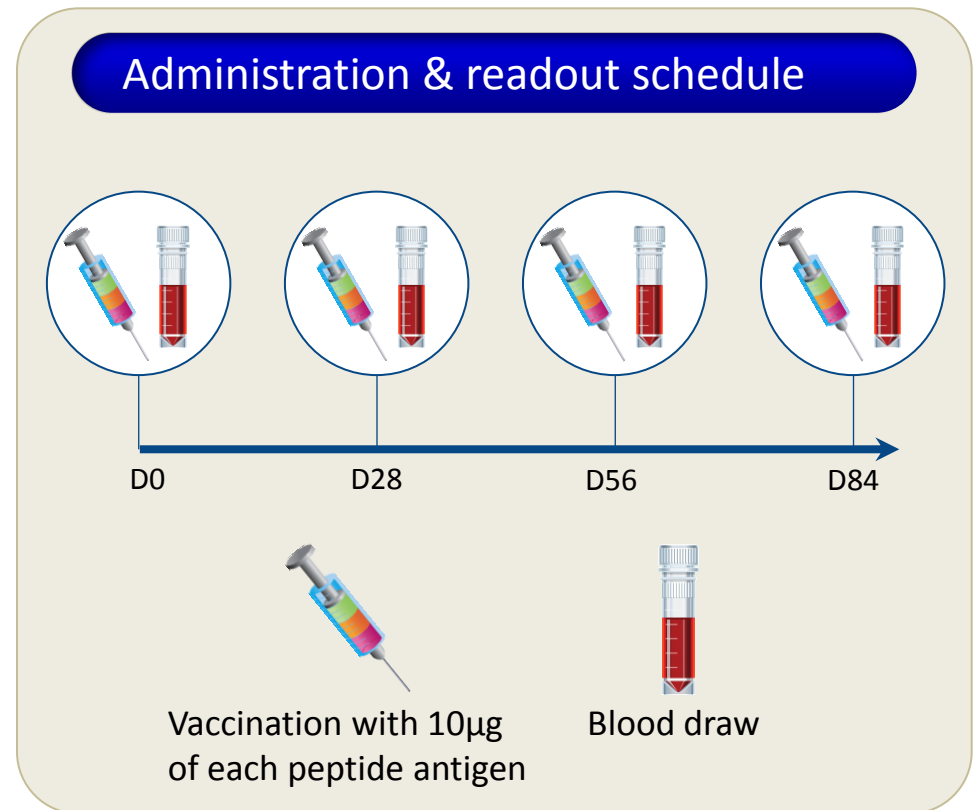
Life expectancy > 4 mo

## Primary endpoint

- Safety & Tolerability

## Secondary endpoint

- Immunogenicity
  - Specific antibodies
  - Cellular responses



PEV06 clinical Phase 1 study

Wiedermann U et al, Breast Cancer Res Treat. 2010

# Phase 1 – Patient Characteristics



## Patients aged 55+ and up to 84 years

Patient ID	Age	Metas. disease since	Prior chemotherapy	Current antihormonal therapy
1	55	Oct. 2006	no	Anastrozol
2	66	May 2004	yes (1 adj)	Fulvestrant
3	84	Mar. 1999	no	Anastrozol
4	79	Sept. 2003	no	Anastrozol
5	67	Apr. 2004	no	Fulvestrant
6	69	Sept. 2004	no	Anastrozol
7	60	Aug. 2002	yes (3 met)	Fulvestrant
8	76	Apr. 1999	no	Fulvestrant
9	63	Jun. 2006	yes (1 met)	Exemestan
10	70	Apr. 2008	No	Anastrozol

Wiedermann U et al, Breast Cancer Res Treat. 2010

# Phase I – Safety and Tolerability

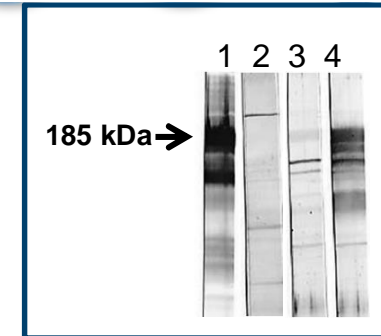
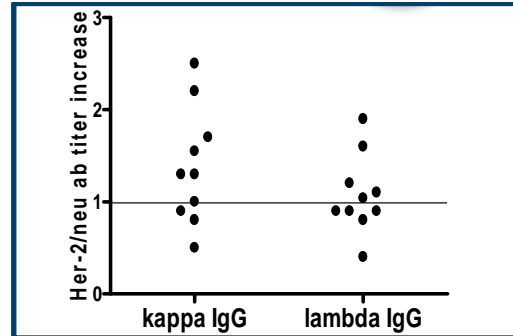
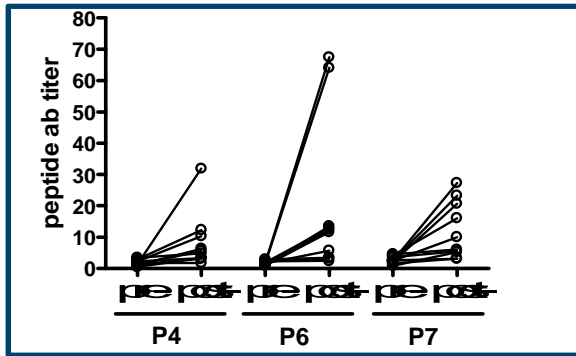


## Few grade 1 local reactions; none systemic

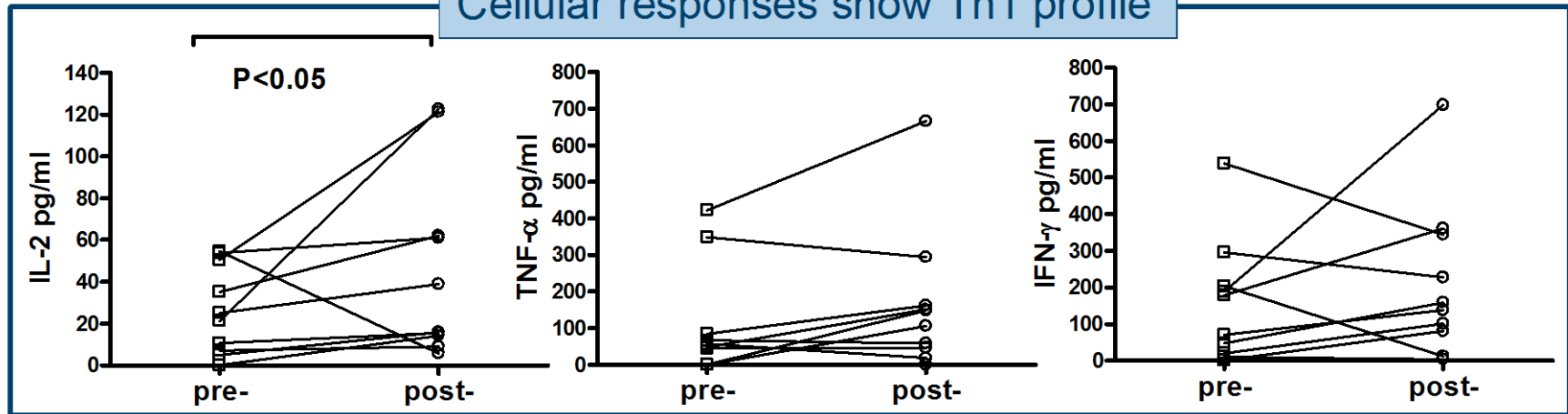
Patient ID	Local vaccination reaction grade	Systemic grade 3/4 toxicity
1	1	no
2	0	no
3	0	no
4	1	no
5	1	no
6	0	no
7	0	no
8	0	no
9	1	no
10	0	no

Wiedermann U et al, Breast Cancer Res Treat. 2010

# Phase I – Secondary Endpoint: Immunologic Responses



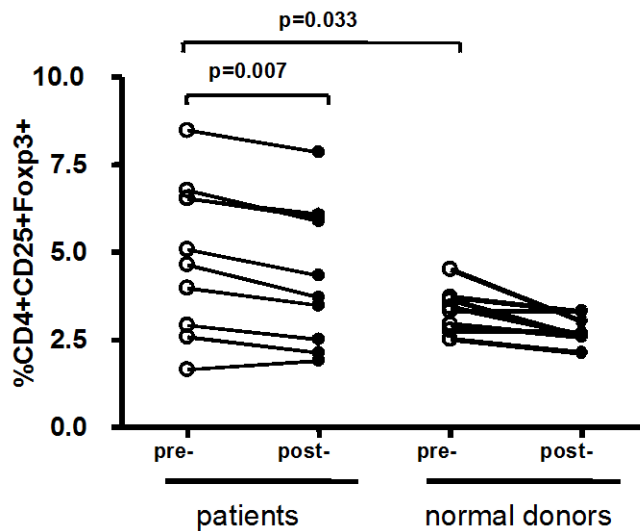
Cellular responses show Th1 profile



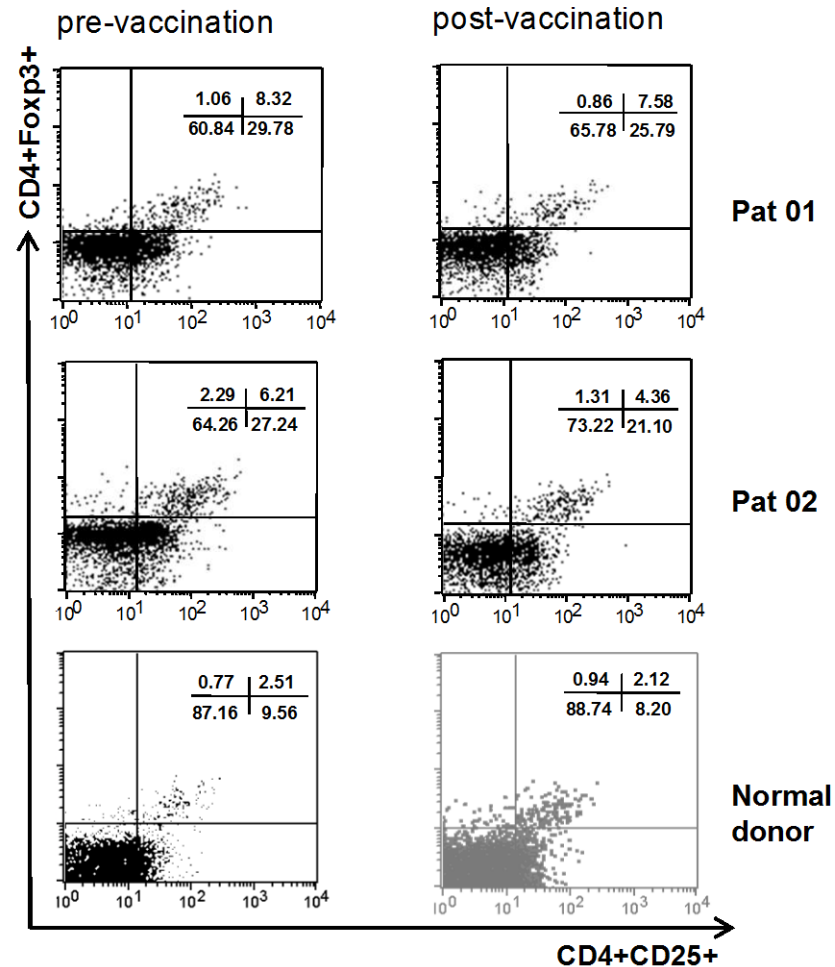
- 8/10 developed significant anti-peptide antibody levels
- In all but one the antibodies were also directed against Her-2/neu
- The majority also showed a 4-fold increase in influenza titers (HHT)16



# Phase I – Regulatory T Cells: Cancer Patients vs. Healthy Controls



- Significantly higher number of CD4+Foxp3+ regulatory T cells in tumour patients than healthy controls
- Vaccination significantly reduced T reg cells in both groups



Wiedermann U et al, Breast Cancer Res Treat. 2010

# Phase 1 HER-Vaxx breast cancer vaccine

## – key developments



- Strong immunogenicity in 8/10 patients in Phase I study with 10 µg of peptide antigen
- Good correlation with cellular responses (cytokines)
- Safe and well tolerated, in particular no cardiotoxicity
- Protective efficacy of peptides demonstrated in preclinical tumor model in mice showing delay of onset and reduced tumor growth

### Antibody and cellular responses in human

Pat. #	Peptide-specific ab P4, P6, P7	HER2-specific ab	Infl. HIT	IL-2, IFN $\gamma$ , TNF	T reg
1	↑ ↑ ↑	↑	-	- - -	↓
2	↑ ↑ ↑	↑	↑	↑ ↑ ↑	↓
3	↑ ↑ ↑	↑ (+/-)	-	↑ - -	↓
4	↑ ↑ ↑	↑	↑	- ↑ ↑	↓
5	↑ ↑ ↑	↑	↑	↑ ↑ ↑	↓
6	- - -	-	-	↓ ↓ ↓	↓
7	↑ ↑ ↑	↑	↑	- - -	↓
8	↑ ↑ ↑	↑ (+/-)	↑	↑ ↑ -	↑
9	↑ +/- +/-	↑	↑	↑ ↑ ↑	↓
10	- - -	-	-	+/- ↓ +/-	↓

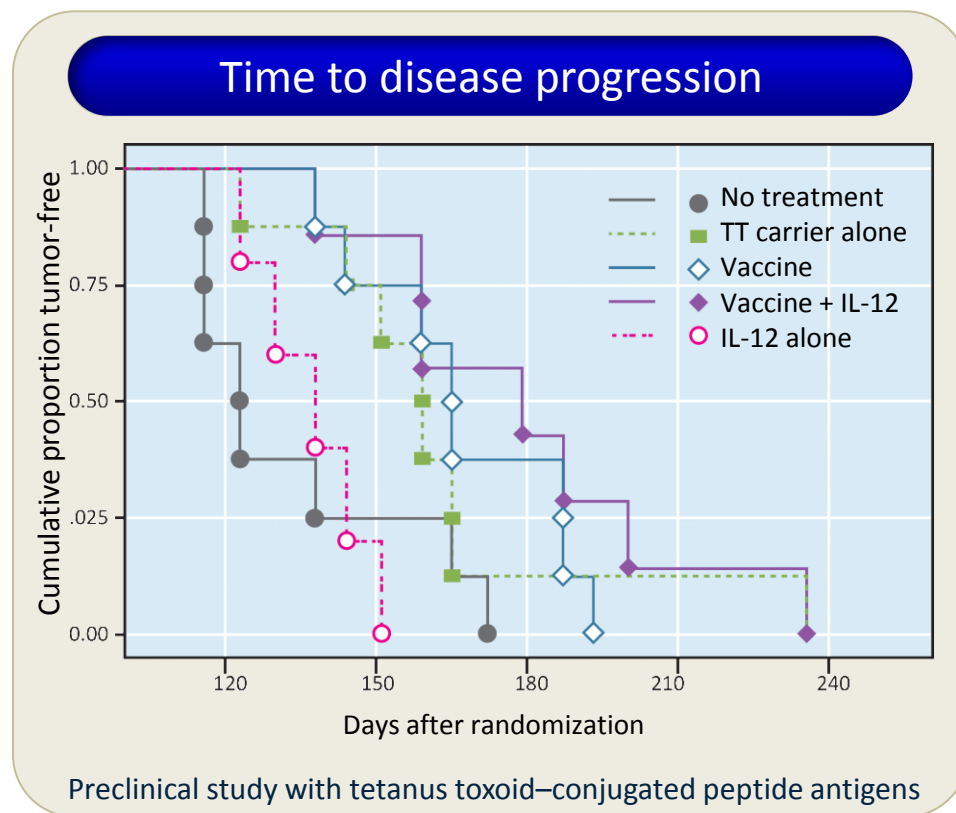
HER-Vaxx breast cancer vaccine – Phase I trial 10 µg group

Excellent immunogenicity even at low dose  
and in patients aged up to 84 years

# Tumor Growth Inhibition *in vivo*



- Prolonged time to disease progression
- Immunization of c-neu transgenic mice (recognized HER2 cancer model) with tetanus toxoid-conjugated peptides P4, P6 and P7
- Vaccinated animals show significant delay in tumor onset and reduced growth kinetics
- Co-administration of IL-12 further improves the vaccine performance



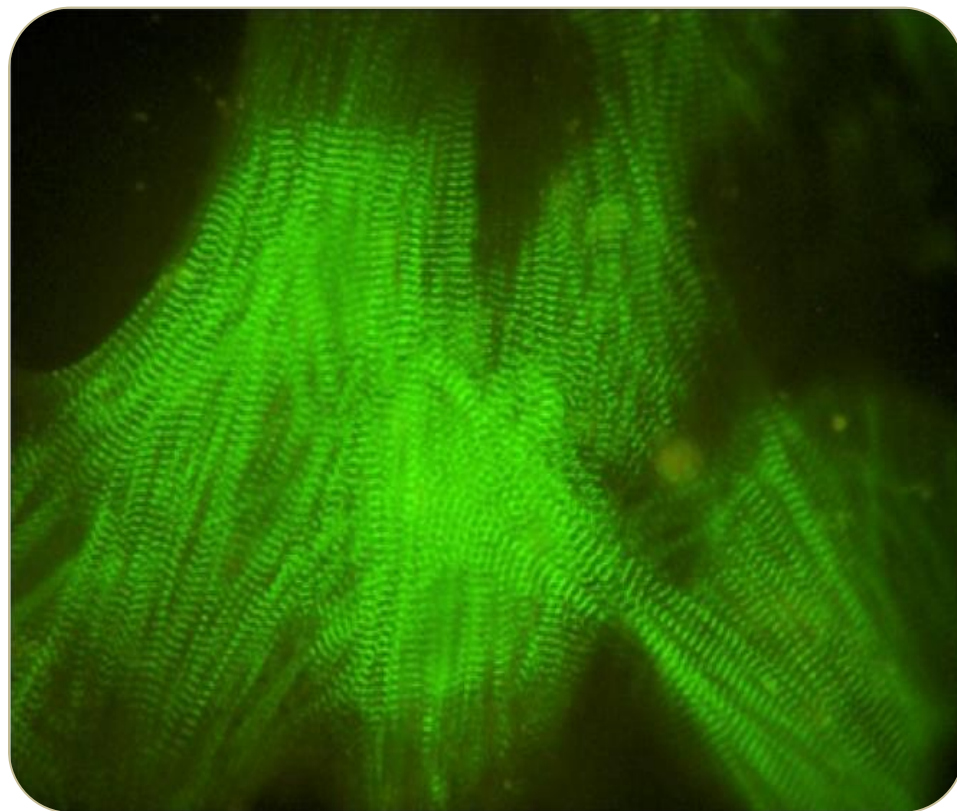
↑  
d 170    ← d 65 →    d 235  
↑

# No toxicity, in particular no cardiotoxicity



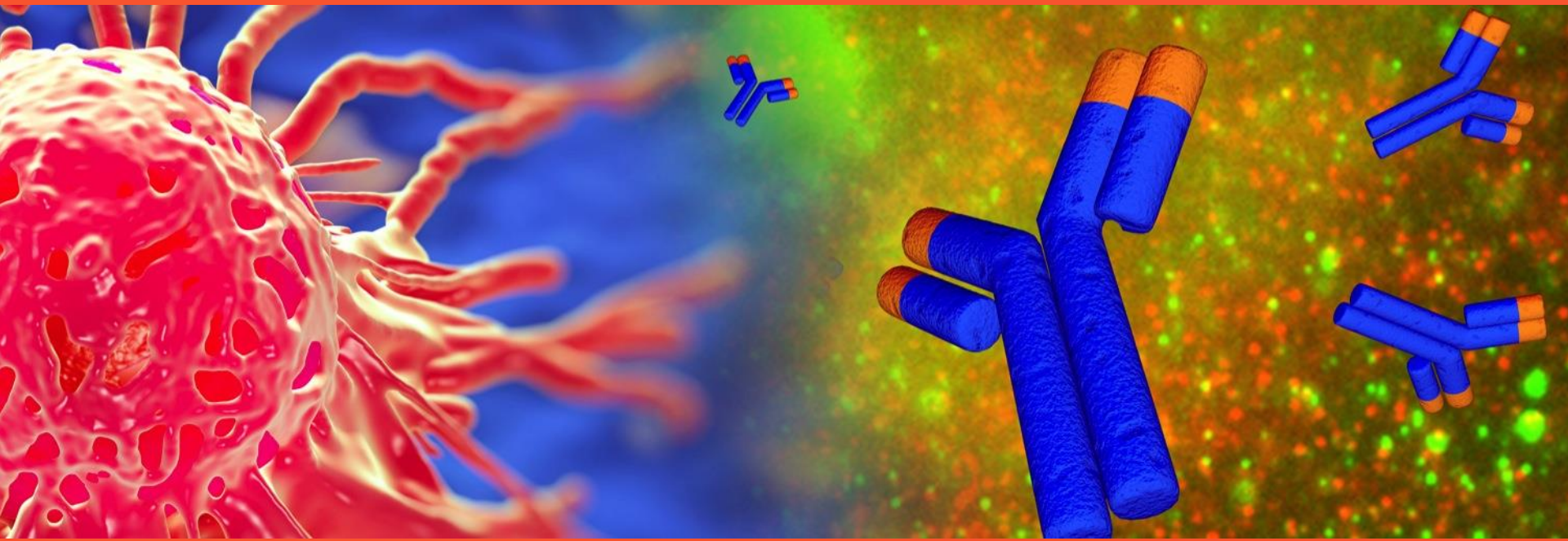
- Repeat dose toxicity study with TT-conjugated peptides in mice
- Repeat dose toxicity study with HER-Vaxx in rats
- Local tolerability & immunogenicity study with HER-Vaxx in rabbits
- In vitro toxicity study with purified serum from immunized animals on rat cardiomyocytes

## Rat cardiomyocytes



*In vitro* toxicity study on rat cardiomyocytes





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