

B Cell Vaccines for Immunotherapy

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Chief Operating Officer
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Why Imugene is Unique



T Cell vaccines have been
exhaustively researched...

...but B Cell vaccines are an open
frontier for immunotherapy

Imugene (ASX: IMU) leading in B
Cell vaccines for immunotherapy

Who is Imugene?



- Leading immunotherapy company, working on B Cell peptide vaccine technology developed at Medical University of Vienna, Austria
- Headquartered in Australia, publicly traded on Australian Securities Exchange (ASX:IMU)
- Lead product, HER-Vaxx, is a HER2 vaccine with Phase 1 in breast cancer completed
- HER-Vaxx moves to Phase 1b/2 in HER2+ gastric cancer in 2016
- Exciting mimotope platform in development at Medical University of Vienna
- Seasoned management team led by Executive Chairman Paul Hopper
- Market capitalisation (1/5/2016) only US\$16.1m (A\$22.5m)
One of the world's best value immunotherapy stocks



ASX

AUSTRALIAN SECURITIES EXCHANGE



MEDICAL
UNIVERSITY
OF VIENNA



B Cell Peptide Vaccine Immunotherapy

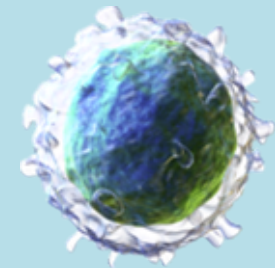


- **Imugene is one of the few biotech companies globally working on B Cell peptide vaccines for immunotherapy**
- Our colleagues at Medical University of Vienna (MUW) have created a HER2 B Cell peptide vaccine, HER-Vaxx, capable of generating a robust anti-cancer polyclonal antibody response
- Imugene and MUW's work on B Cell peptide vaccines is focused on discovering the potential to improve performance and cost effectiveness of monoclonal antibodies
- In the Era of Immuno-Oncology, B Cell peptide vaccines has a potential to play an important role
- We believe we have the management team to position B Cell peptide vaccines as a clinically relevant immunotherapy

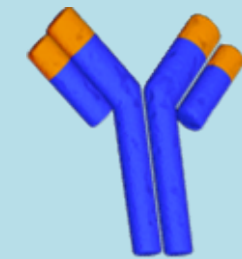
Why B Cell Vaccines?



- **No HLA restriction**
- Potential for higher affinity and specificity polyclonal antibodies than monoclonals, depending on epitope conformation
- Potential for additional and superior antitumor effects through targeting different biologically relevant regions for the cancer in question
- ADCC (Antibody dependent cell mediated cytotoxicity) and CDC (complement dependent cytotoxicity) as per monoclonals, but at much lower cost
- T Help can come from vaccine formulation
- Generation of immune memory
- Potentially less toxicity
- Combining several B-cell epitopes into a single antigen is synergistic and results in a stronger immune response



B Cell



Antibody

Why Our B Cell Peptide Vaccines?



Epitope discovery technologies

- Allows most antigenic epitopes to be identified



2010 - First generation vaccine performed very well in the clinic

- Target-specific antibodies with potent anti-tumor activity
- Reduction in Treg cells post-vaccination
- Induction of cytokines (Th1 biased, IFN- γ production)
- Induction of memory T & B cells



2016 - Third generation vaccine goes to clinic

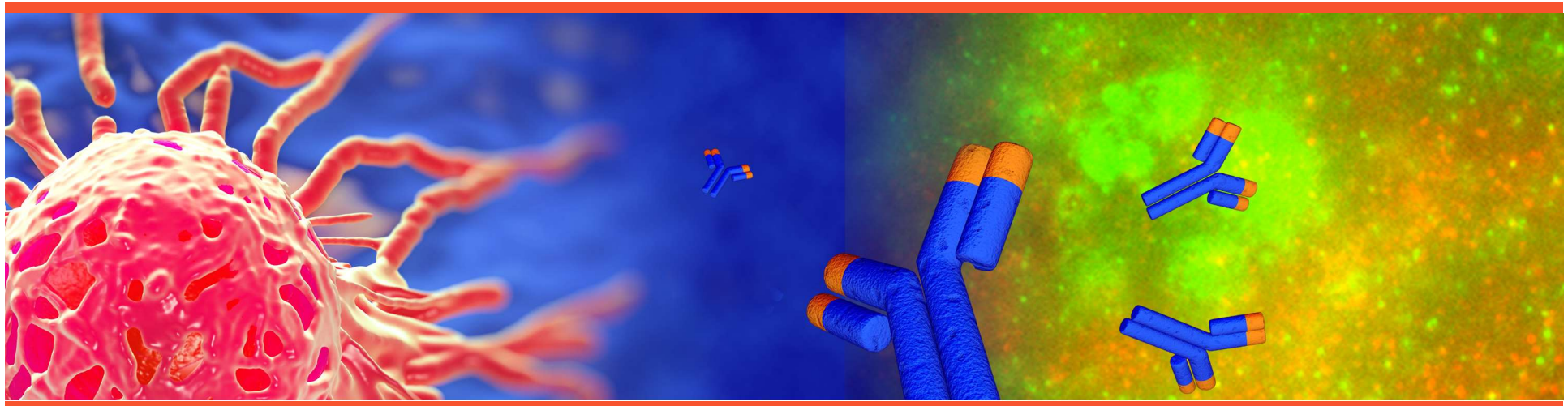
- Single peptide
- CRM197 carrier system easier to make
- Significantly higher antibody titre *in vivo*

Why Imugene?



- **Compelling science** both for HER-Vaxx and mimotopes
- **Leadership** – Experienced management led by Executive Chairman Paul Hopper (Polynoma, Viralytics); the board owns 6%
- **Validated target for first product** – HER-Vaxx targets same receptor as Roche's ~\$8bn Herceptin and Perjeta franchise
- **Phase 1 completed** – Anti-HER2 antibody responses, T helper cytokines, Treg cells suppressed, therapy safe
- **Robust IP** – Exclusivity for HER-Vaxx until at least 2030 on granted US and EU patents - further patent life extensions to 2036 and beyond underway
- **News flow** – Numerous milestone announcements and valuation inflection points over next 12-24 months

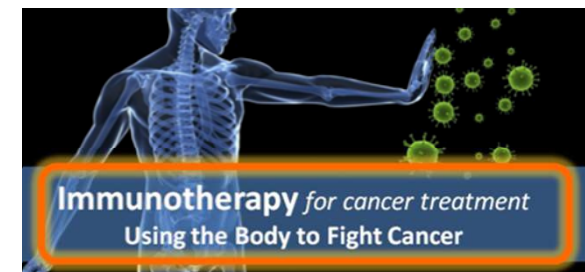
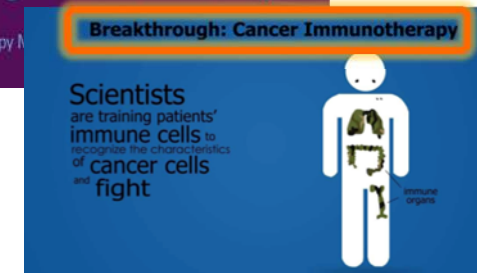
B Cell Peptide Vaccines in the Era of Immuno-Oncology



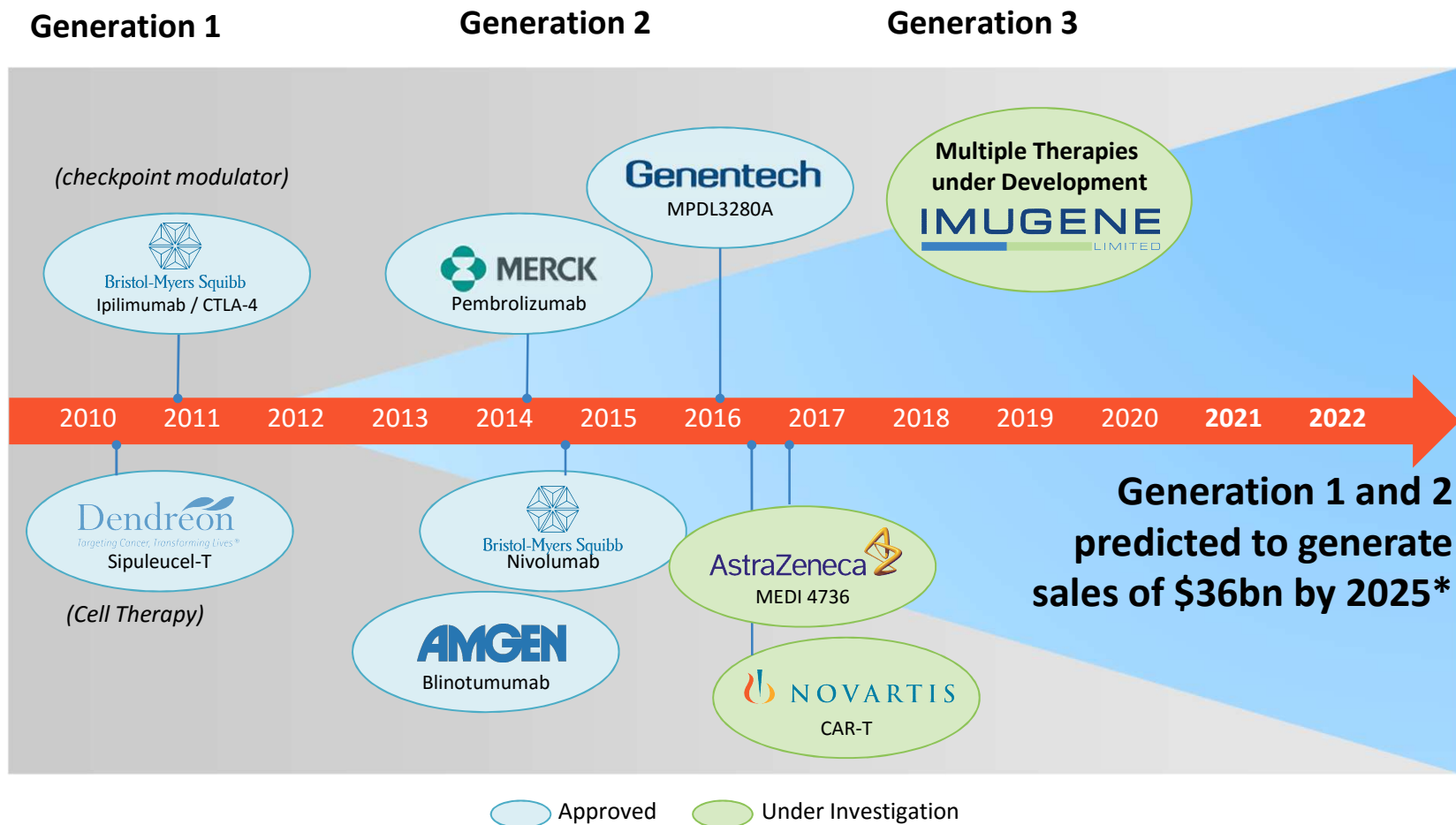
Imugene Operates in The Most Promising Area of Oncology Today...



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

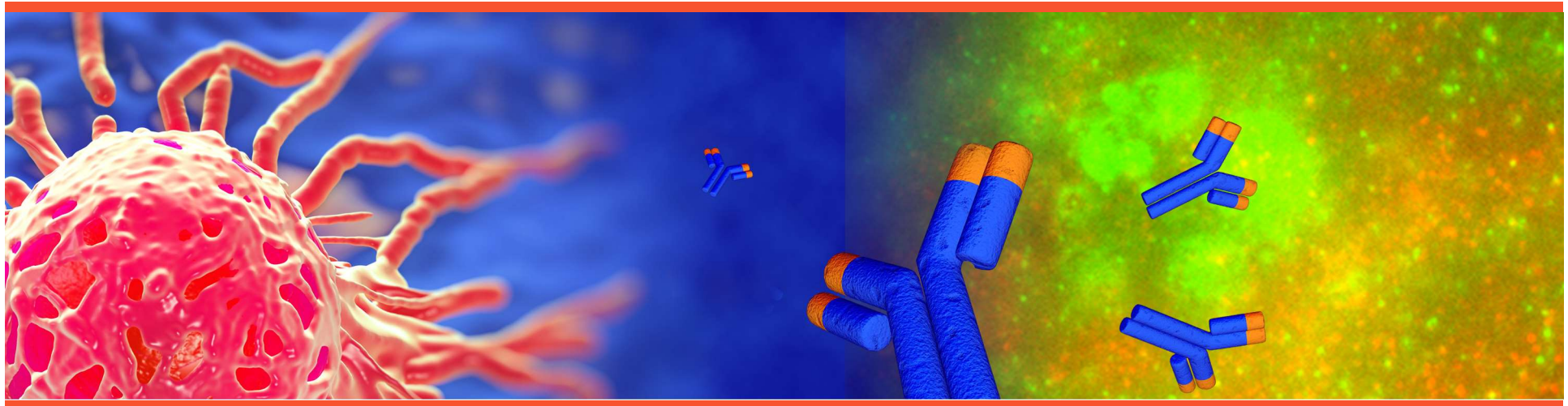


The Immunotherapy Breakthroughs of the Last Five Years are Helping to Shape our Market Opportunity



*Citigroup research note

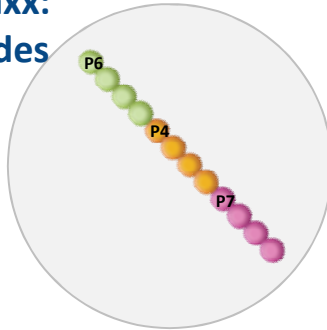
HER-Vaxx – a Potential Breakthrough B Cell Peptide Vaccine



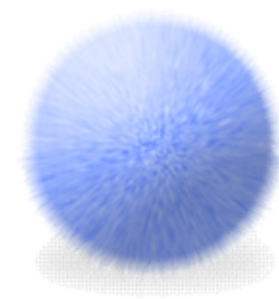
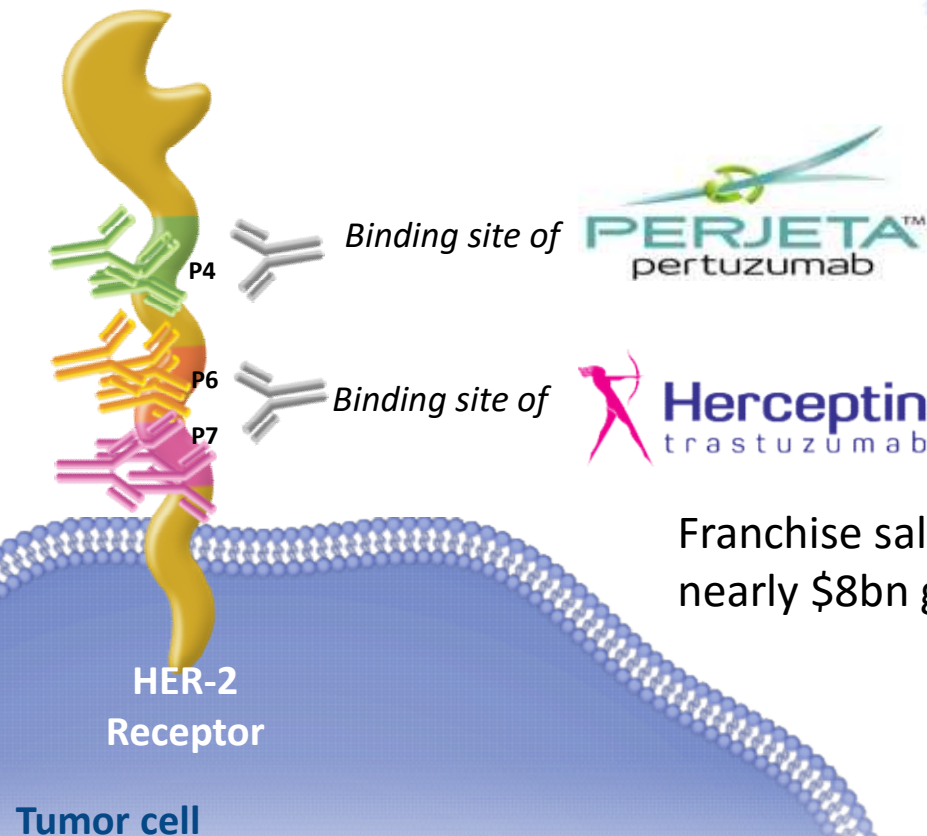
HER-Vaxx Attacks the same Cancer Receptor the World's Largest Cancer Franchise



HER-Vaxx:
3 peptides



HER-Vaxx: x3
polyclonal
responses



Monoclonal
response

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

* \$USD Source: Roche H1 Report <http://www.roche.com/hy15e.pdf> p12



HER-Vaxx is a Differentiated Product



- 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 γ 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

Phase Ia In Breast Cancer, Conducted at Medical University of Vienna, Demonstrated Immunogenicity*



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

Results

- Patients developed anti-HER-2 Abs
- Induction of cytokines (Th1 biased; IFN γ)
- 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
- Promising results - Patients were end stage and not primary target group



* Wiedermann et. al., Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

HER-Vaxx Has Been Considerably Optimised Since Phase 1a



First Generation

- (used in Phase 1a) was three separate B Cell epitopes delivered in virosomes

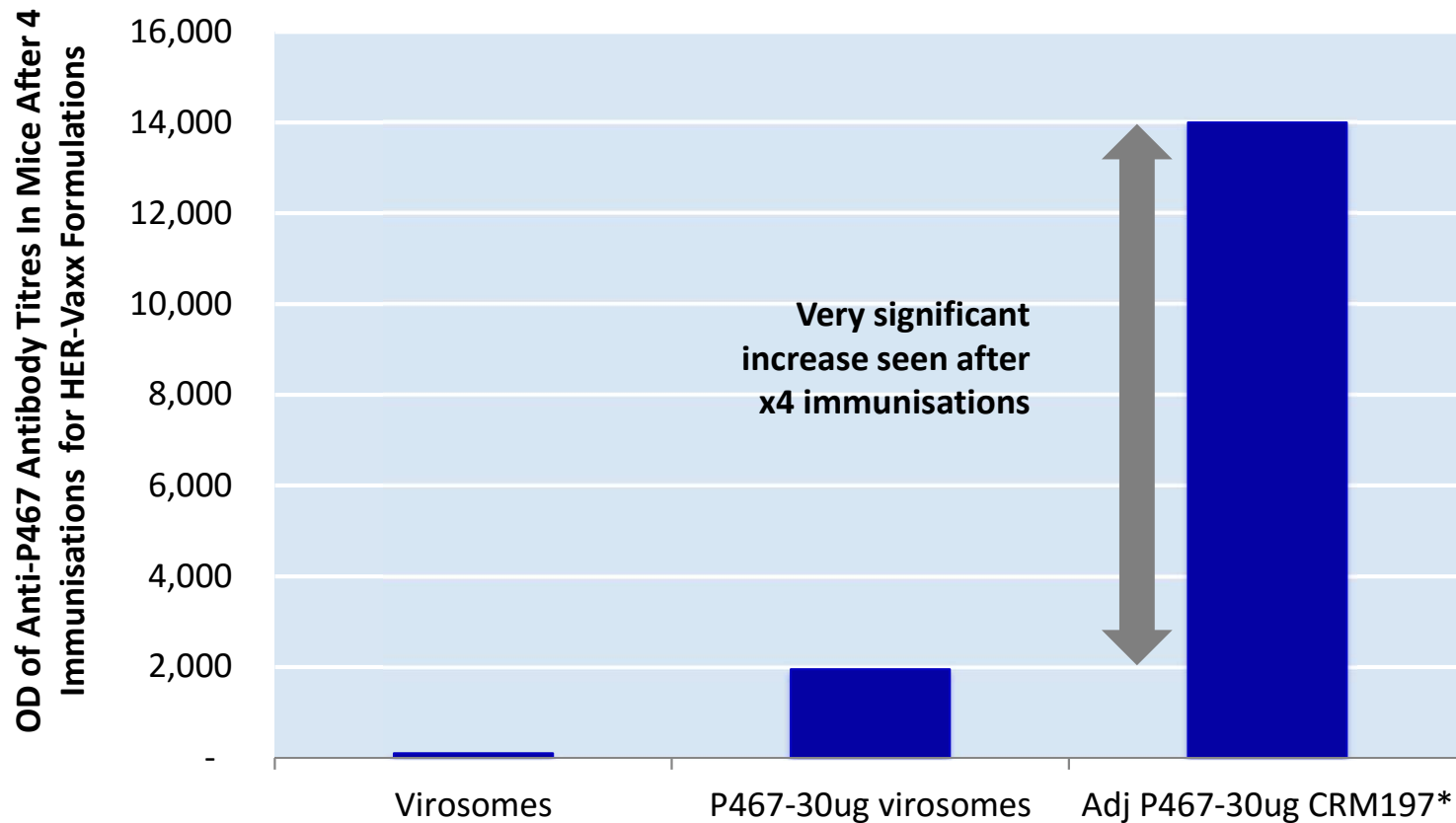
Second Generation

- incorporated the three B Cell epitopes into a single 49-mer peptide
- > 2x increase in antibody response *in vivo* compared to three single epitopes (extended patent life to 2030)

Third Generation

- changed the delivery system from virosomes to CRM197 (which gave CD4 T-Help response), and added an adjuvant
- >10x increase in antibody response *in vivo* (potentially extends patent life to 2036)

HER-Vaxx 3G Registers Markedly Increased Antibody Titres



* Data adjusted for comparison; original data generated for P467-30ug CRM197 generated with 1/20th of the concentration of comparable virosome formulation. Adjustment may be subject to variation

NOTE: Actual antibody levels vary depending on number of immunisations, dose used and characteristics of antibodies under observation.

Phase 1b/2, Starting 2016 Under an IND, in HER2+ Gastric Cancer



Phase 1b lead-in

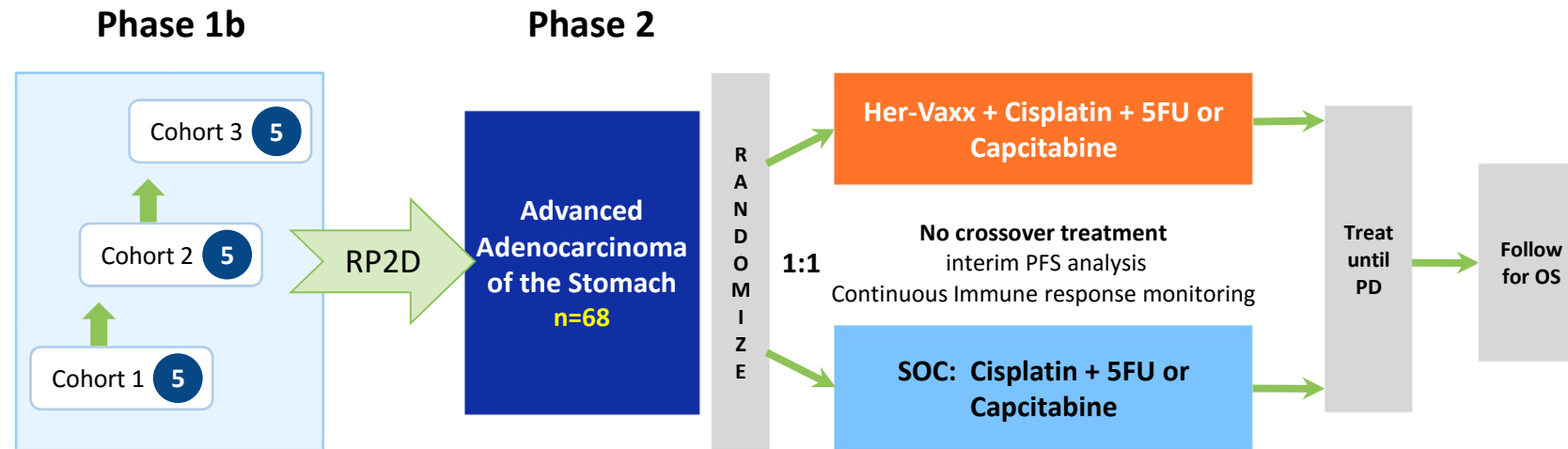
- Open label
- 15 patients, x3 groups of 5 patients
- Combination with chemo
- Endpoints:
 - RP2D (Recommended Phase 2 Dose) of HER-Vaxx
 - Safety: any HER-Vaxx toxicity
 - Immunogenicity (anti-HER-2 antibody titres)
 - Test booster schedule (q 4 weeks or 8 weeks)

Phase 2

- Open label
- ~68 patients from sites in Asia
- Combination with chemo
- Randomized
- Primary Endpoints:
 - Overall Survival
 - Progression-Free Survival
- Secondary endpoint:
 - Immune response

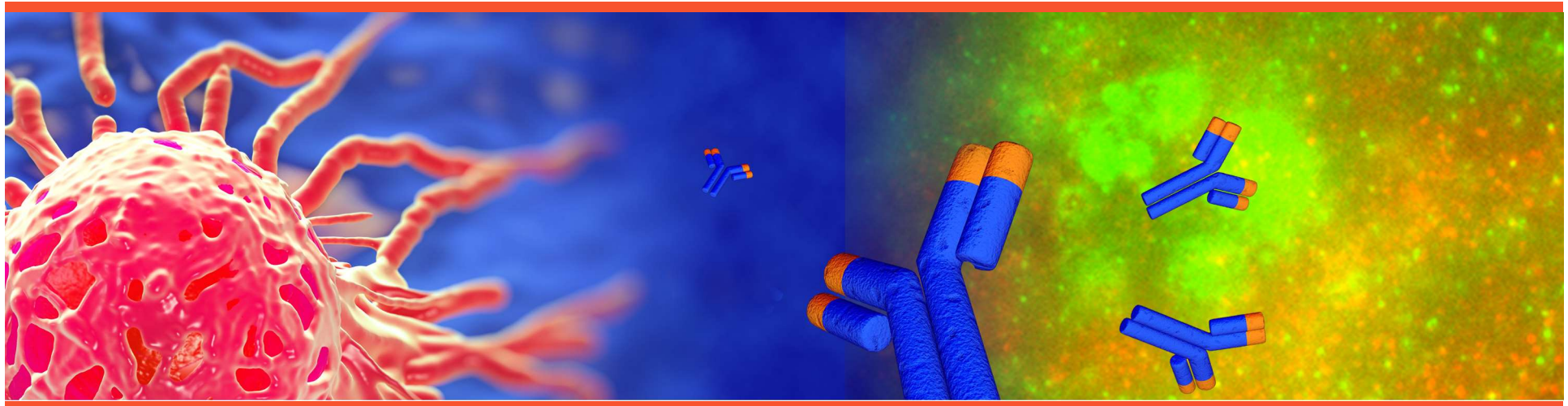


Phase 1b/2 Trial Design Gastric Cancer



Design	Phase 1b/2
IND Submission	Q1, 2016
Final Protocol	Q1, 2016
N	Phase 1b =15; Phase 2 = 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	Central Lab

Mimotopes – Delivering on the Promise of B Cell Peptide Vaccines



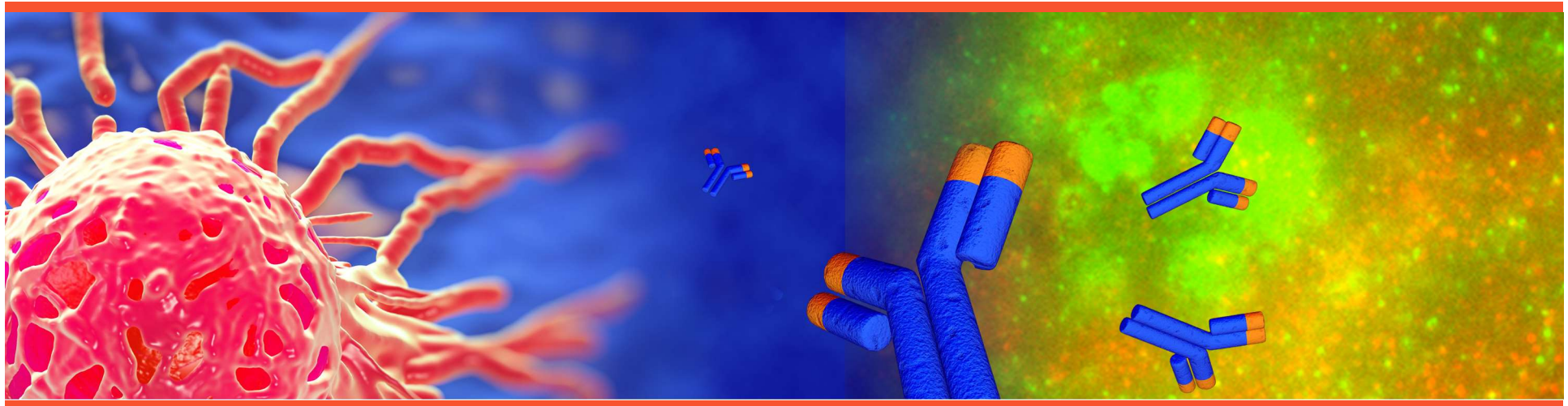


With our mimotopes technology, we can reverse-engineer monoclonal antibodies



- Our colleagues at Medical University of Vienna have developed cutting edge proprietary techniques to select peptides that would mimic monoclonal antibodies
- Imugene has acquired an option to develop mimotope vaccines with MUW.
- We believe mimotopes will be part of the next wave of the Immunology Revolution
- In conjunction with the MUW team we are now selecting novel vaccine candidates against a variety of cancer targets
- This greatly extends the Imugene's oncology franchise and pipeline

The Imugene value proposition



Compelling science and commercial opportunity



HER-Vaxx

- Strong antibody response
- T Regs down
- Tumor growth inhibition *in vivo*
- Induction of cytokines, inc. IFN γ
- Induction of memory T & B cells post vaccination
- IP life out to 2030 and beyond
- Existing HER2 franchise now US\$8bn and growing

Mimotopes

- Various proprietary technologies allows suitable B cell epitopes to be identified
- Monoclonal antibody market now >US\$60bn pa

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*

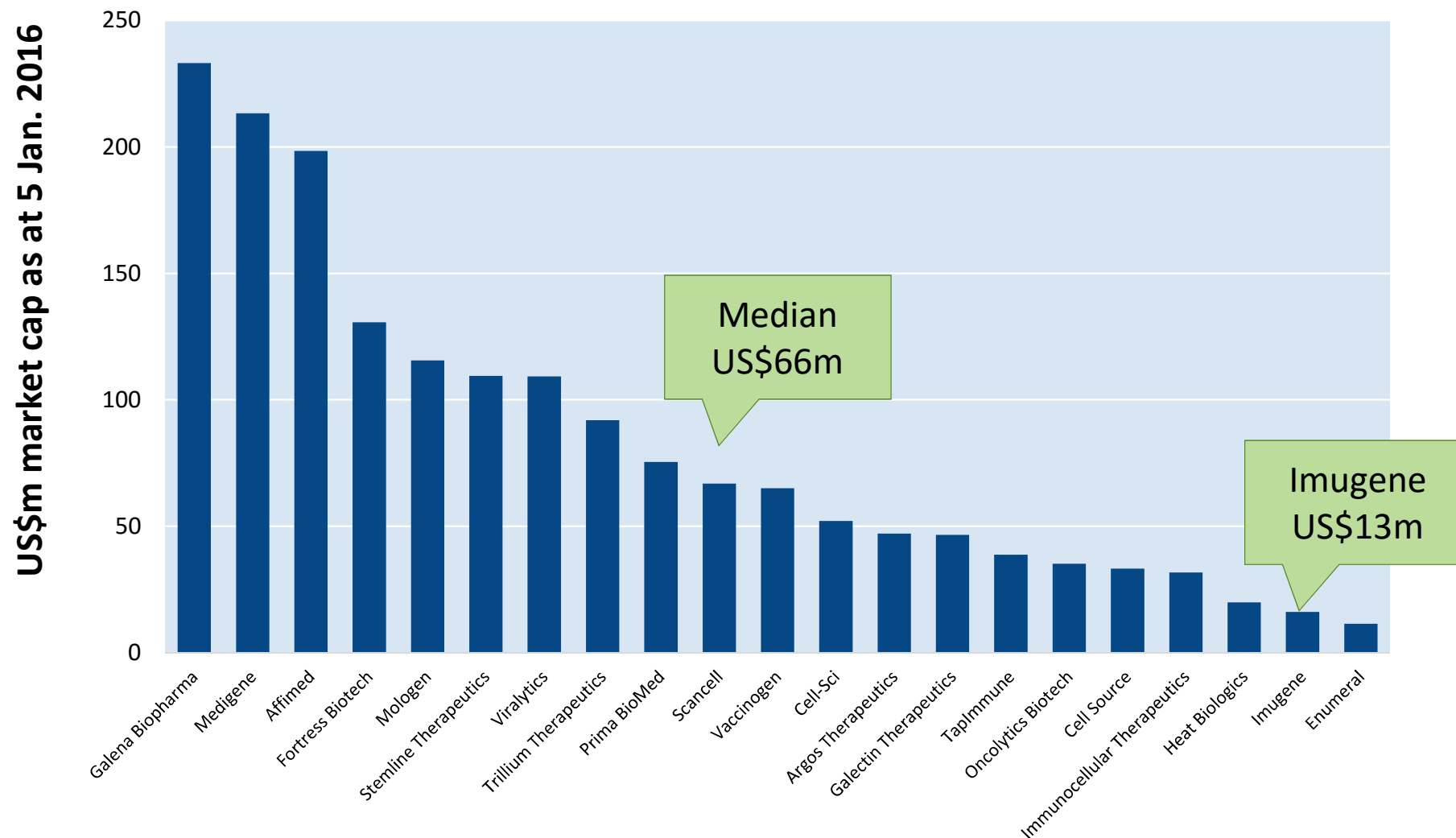
- Former CTO Consegna, CEO Adistem Ltd, CEO Mimotopes P/L, COO EQiTX Ltd (ZingoTX & VacTX)
- VP Chemistry Chiron (now Novartis), Research Fellow CRC Vaccine Technology



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

Attractive Valuation



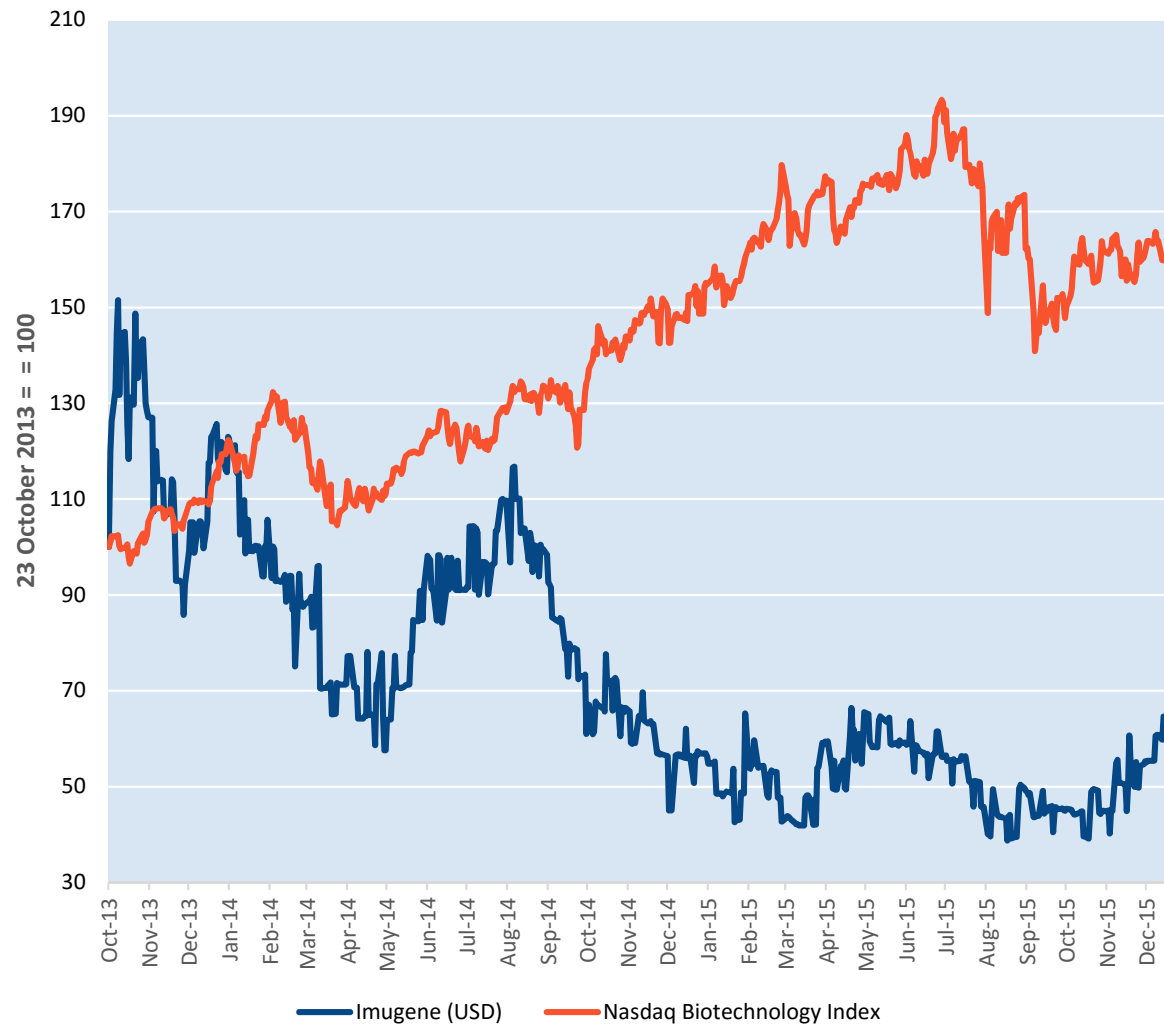
Our Stock Has Stabilised Since Mid-2015



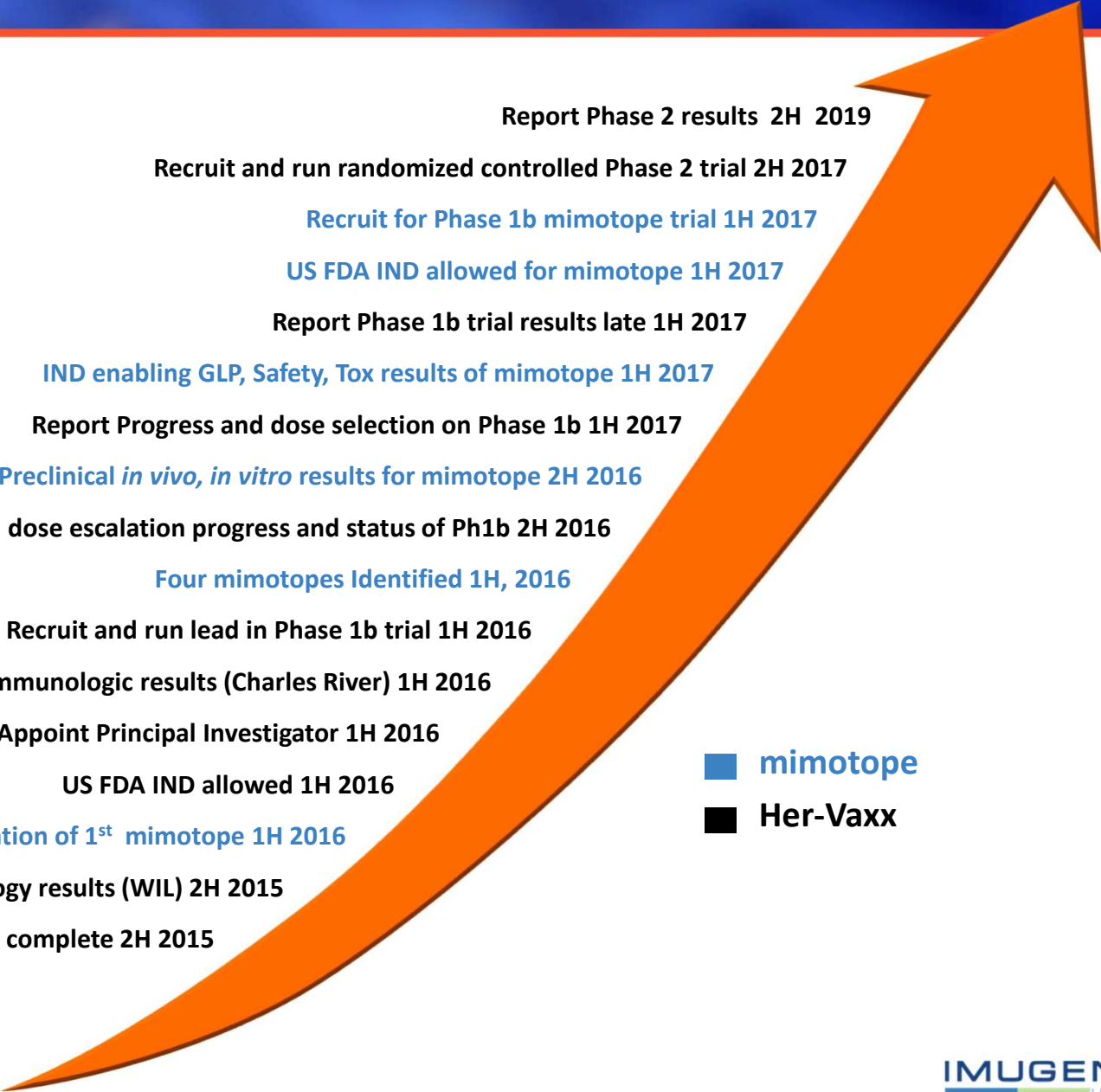
- Company spent 2014 and 2015 preparing second and third generation HER-Vaxx

HOWEVER

- We are now going to the clinic in 2016
- We expect strong news flow
- There is potential for strong progress with our mimotopes program



Strong News Flow



Report Phase 2 results 2H 2019

Recruit and run randomized controlled Phase 2 trial 2H 2017

Recruit for Phase 1b mimotope trial 1H 2017

US FDA IND allowed for mimotope 1H 2017

Report Phase 1b trial results late 1H 2017

IND enabling GLP, Safety, Tox results of mimotope 1H 2017

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

Preclinical *in vivo*, *in vitro* results for mimotope 2H 2016

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

Four mimotopes Identified 1H, 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

Identification of 1st mimotope 1H 2016

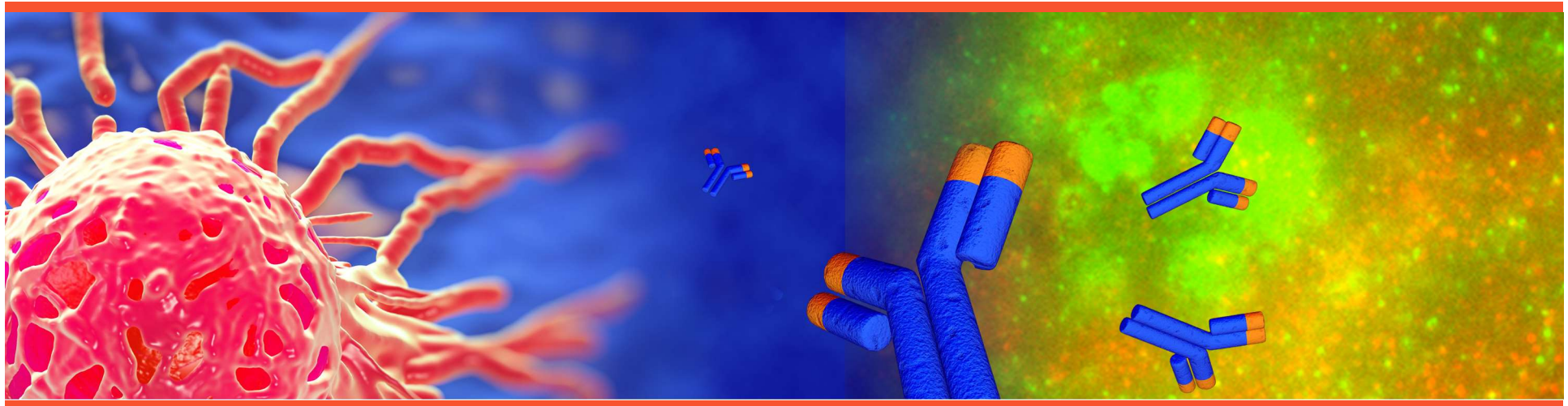
Announce preclinical toxicology results (WIL) 2H 2015

Her-Vaxx GMP clinical batch complete 2H 2015

■ mimotope

■ Her-Vaxx

B Cell Vaccine Immunotherapy



Our Stock



ASX:IMU, ISIN: AU000000IMU9

Market Cap (1/52016)	\$22.5M AUD, \$16.5M USD
Ordinary Shares	1.73 billion
12 month price range	0.8 cents – 1.7 cents AUD
Avg daily volume	2.28M shares (last three months)
Public Equity Invested to date	\$9.00M
Cash & Equivalents	\$4.3M (as at Sep '16, include 3.0M raise)

Options on issue (as at Jan. 2016)

	No of options	Exercise Price	Expiry
Listed (IMUO)	371,177,356	\$0.015	31-Mar-17
Unlisted	109,000,000	\$0.0173*	30-Oct-17*
TOTAL	480,177,356	\$0.0155*	18-May-17*

Substantial holders as at Jan. 2016

	No. of Shares	% Capital
Otto Buttula	107,000,000	6.2
Tom Henderson	89,666,666	5.2
Paul Hopper	71,196,875	4.1

* Average



Thank you

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Paul Hopper

Executive Chairman

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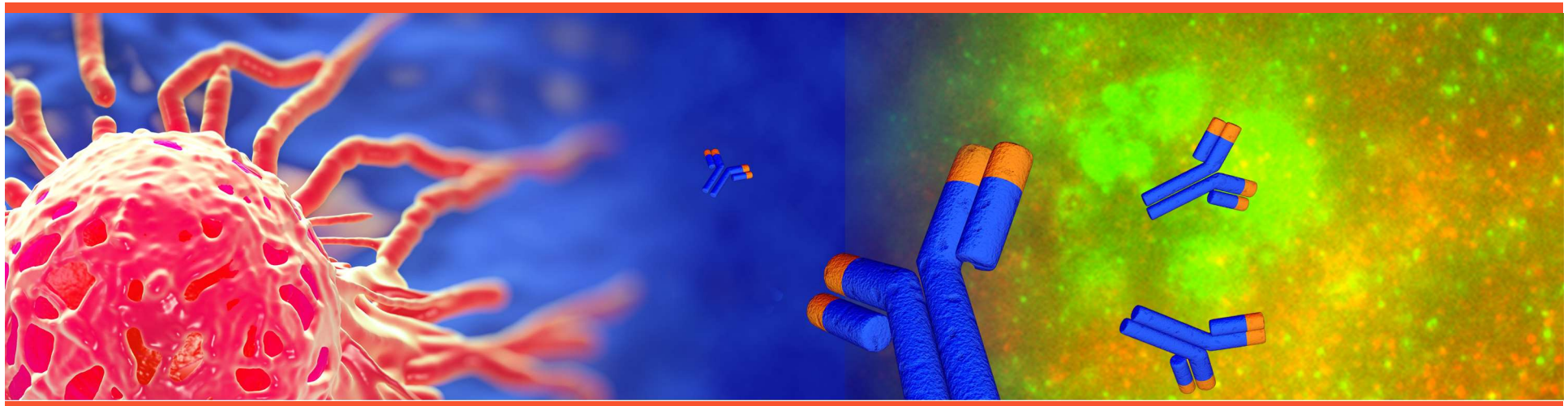
Stuart Roberts

Head of Corporate Development

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Appendix – HER-Vaxx Phase 1 Results



Study Design*



Patient inclusion criteria

- Metastatic breast cancer
- HER2 +, ++
- ER/PR pos.
- Life expectancy > 4 mo

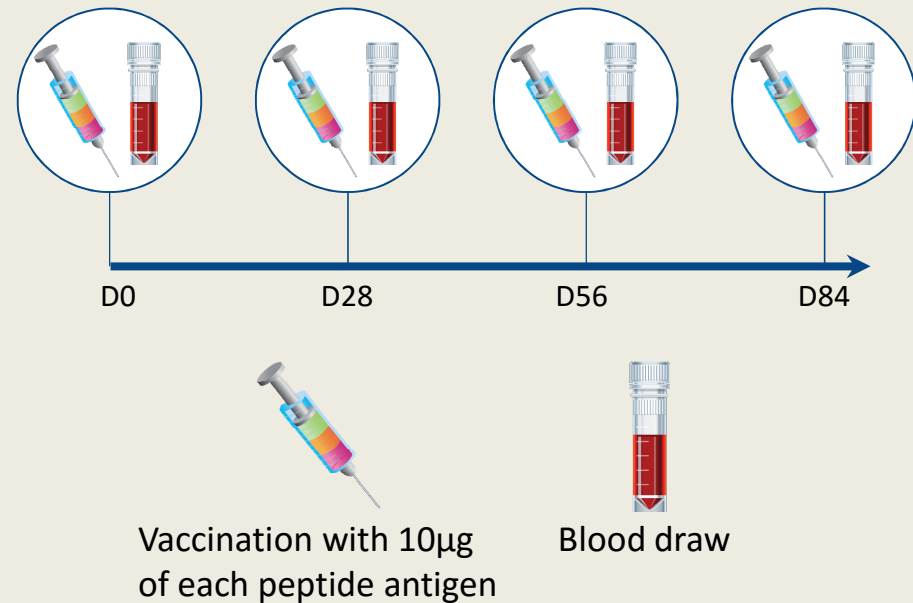
Primary endpoint

- Safety & Tolerability

Secondary endpoint

- Immunogenicity
 - Specific antibodies
 - Cellular responses

Administration & Readout Schedule



* Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

Patient Characteristics – Aged 55-84 *



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

* Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

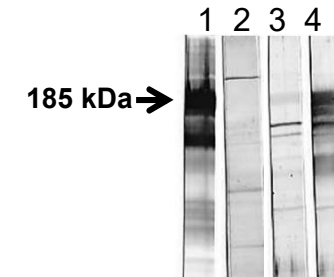
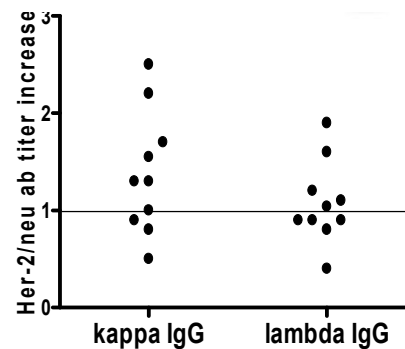
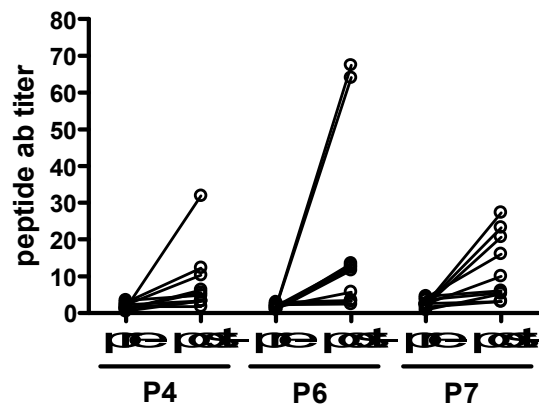
Safety and Tolerability - Few Grade 1 Local Reactions, None Systemic*



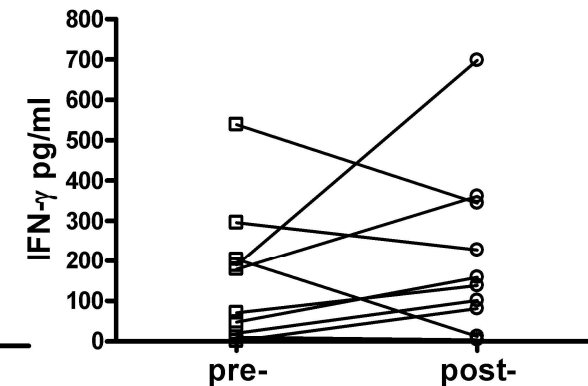
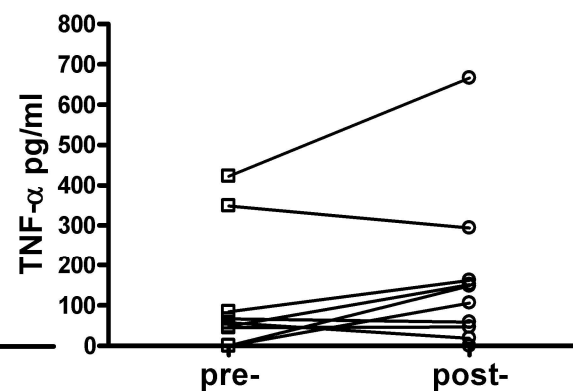
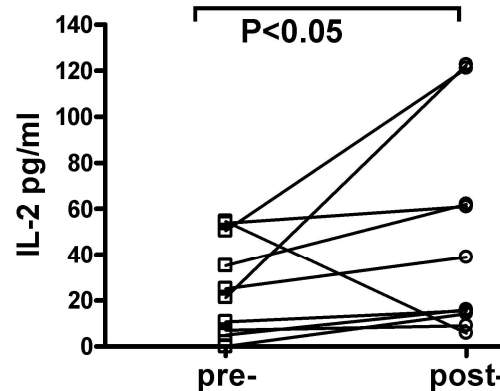
Patient ID	Local vaccination reaction grade	Systemic grade 3/4 toxicity
1	1	no
2	0	no
3	0	no
4	1	no
5	1	no
6	0	no
7	0	no
8	0	no
9	1	no
10	0	no

* Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

Phase 1 Secondary Endpoint – Immunologic Responses

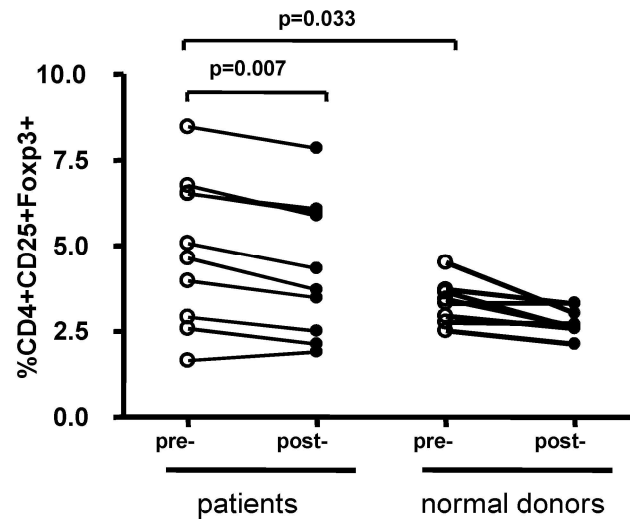


Cellular responses show Th2 profile

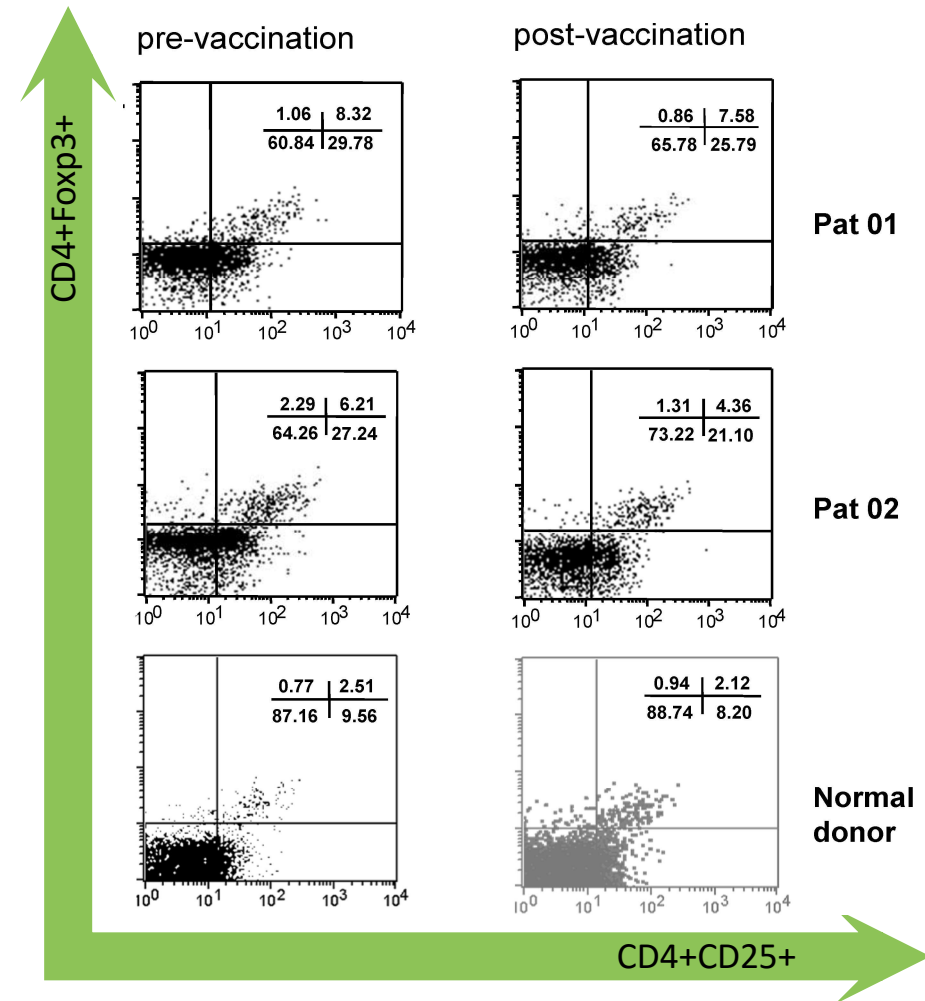


- 8/10 developed significant anti-peptide antibody levels
- In all but one the antibodies were also directed against Her-2/neu
- The majority also showed a 4-fold increase in influenza titres (HI)

Reduction in Regulatory T Cells*



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



* Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

Excellent Immunogenicity, even at low dose, and in Patients aged up to 84 years, with no Cardiotoxicity

- Strong immunogenicity in 8/10 patients in Phase 1 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

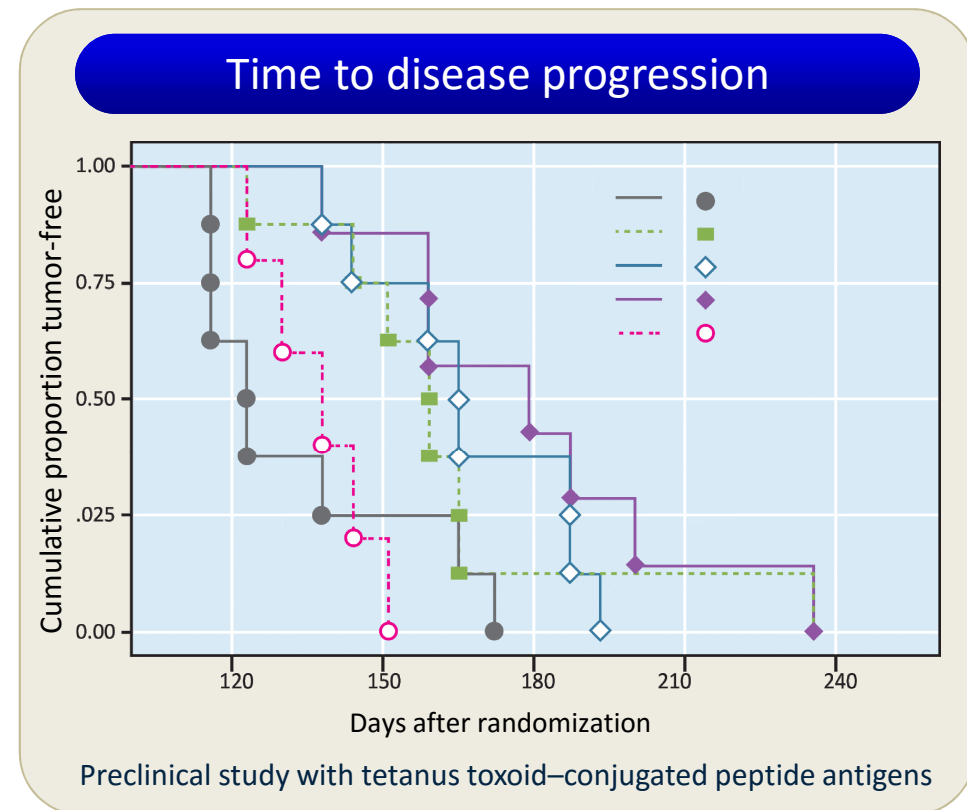
Pat. #	Peptide-specific ab P4, P6, P7	HER2-specific ab	Infl. HIT	IL-2, IFN γ , TNF	T reg
1	↑ ↑ ↑	↑	-	- - -	↓
2	↑ ↑ ↑	↑	↑	↑ ↑ ↑	↓
3	↑ ↑ ↑	↑ (+/-)	-	↑ - -	↓
4	↑ ↑ ↑	↑	↑	- ↑ ↑	↓
5	↑ ↑ ↑	↑	↑	↑ ↑ ↑	↓
6	- - -	-	-	↓ ↓ ↓	↓
7	↑ ↑ ↑	↑	↑	- - -	↓
8	↑ ↑ ↑	↑ (+/-)	↑	↑ ↑ -	↑
9	↑ +/- +/-	↑	↑	↑ ↑ ↑	↓
10	- - -	-	-	+/-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

HER-Vaxx breast cancer vaccine – Phase 1 trial 10 µg group

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
↑

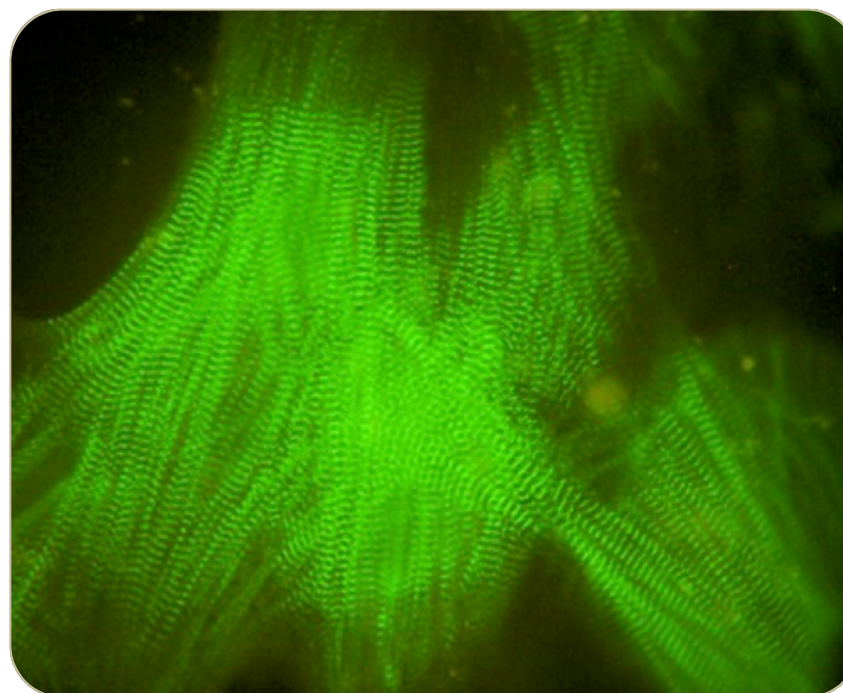
* Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

No toxicity, in particular no cardiotoxicity



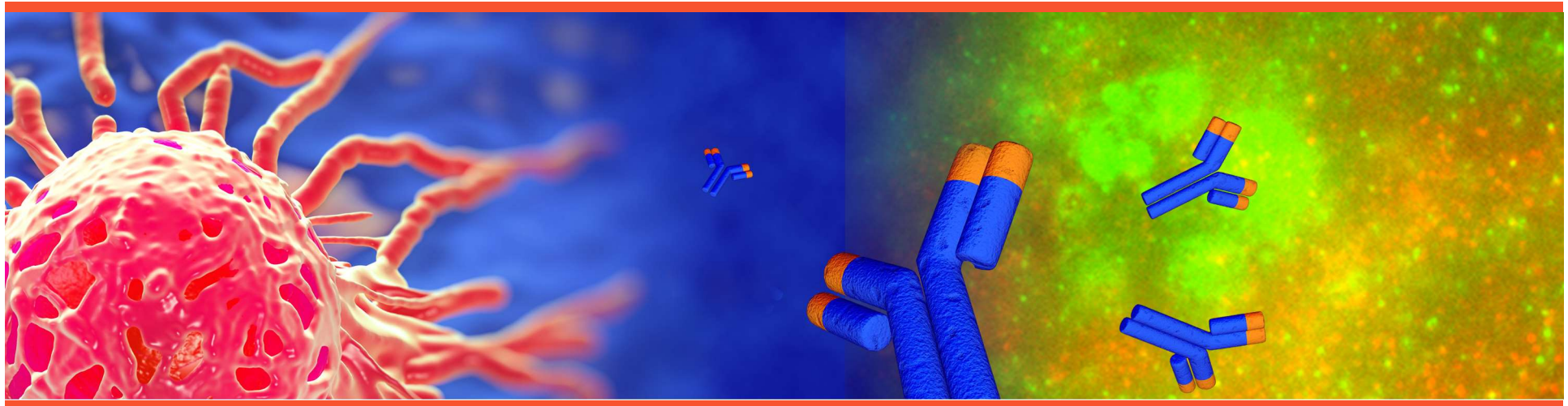
- Repeat dose toxicity study with TT-conjugated peptides in mice
- Repeat dose toxicity study with HER-Vaxx in rats
- Local tolerability & immunogenicity study with HER-Vaxx in rabbits
- In vitro toxicity study with purified serum from immunized animals on rat cardiomyocytes

Rat cardiomyocytes



In vitro toxicity study on rat cardiomyocytes

B Cell Vaccine Immunotherapy



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