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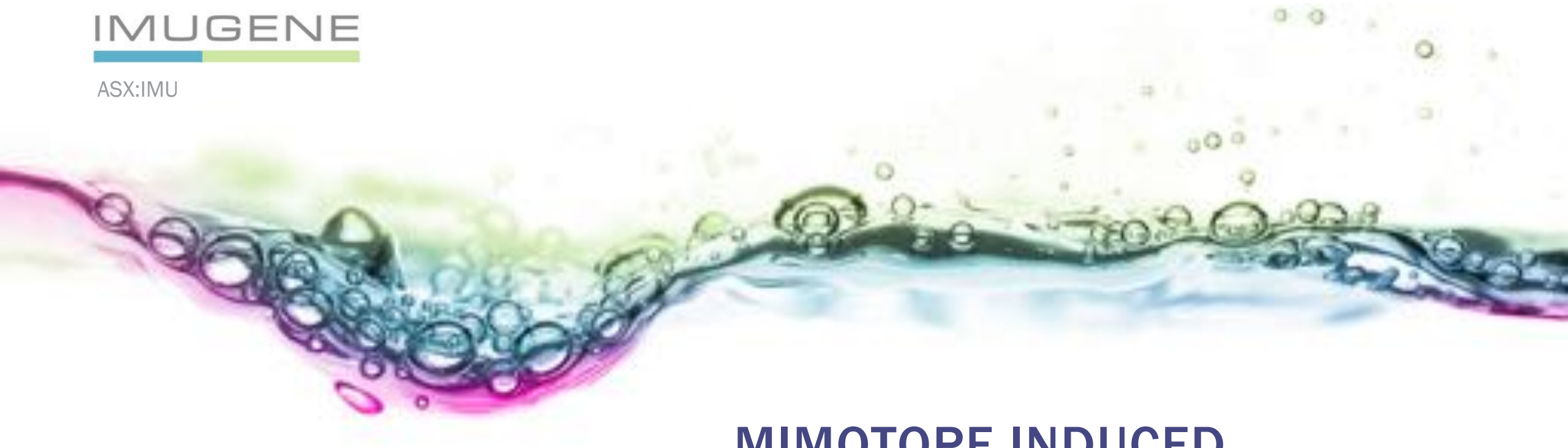

# MIMOTOPE INDUCED B-CELL ANTIBODIES FOR IMMUNO-ONCOLOGY

Leslie Chong | Chief Executive Officer

January/2018

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# NOTICE: FORWARD LOOKING STATEMENTS

Any forward looking statements in this presentation have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside Imugene Limited's control. Important factors that could cause actual results to differ materially from any assumptions or expectations expressed or implied in this brochure include known and unknown risks. As actual results may differ materially to any assumptions made in this brochure, you are urged to view any forward looking statements contained in this brochure with caution. This presentation should not be relied on as a recommendation or forecast by Imugene Limited, and should not be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

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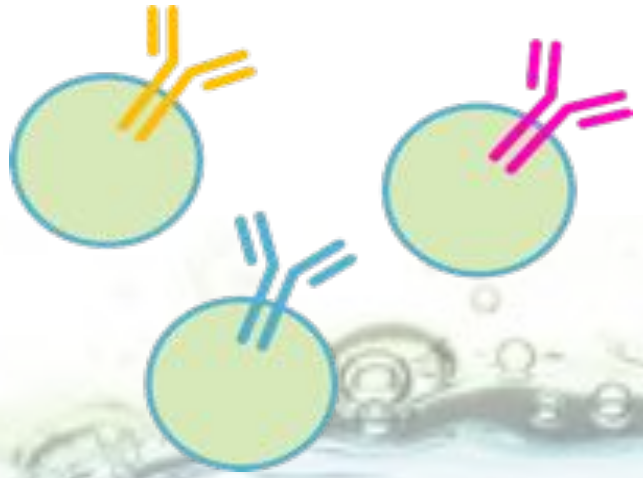
# EXECUTIVE SUMMARY

- Experienced management & board
- Novel oncology platforms: Mimotopes: B cell peptide vaccines – IP protected to 2036
- Lead mimotope: HER-Vaxx Phase 1b/2 mimotope study in Her2+ gastric cancer (large unmet medical need by current existing therapies)
  - POC demonstrated in Phase 1 Her-2+ breast cancer study – safety & immunogenecity established
- Discovery Pipeline:  Mimotope candidate selection and Arginine modulators in pre-clinical development



# WHAT DOES IMUGENE DO?

Imugene's technology
can induce a patient's body
to make its own specific
antibodies that target cancer.

# A TEAM WITH TRACK RECORD IN DRUG DEVELOPMENT

## Leslie Chong (Sydney, Australia)

Chief Executive Officer

- Over 19 years of oncology experience in Phase I - III of clinical program development
- Leadership role involvement in 2 marketed oncology products
- Previously Senior Clinical Program Lead at Genentech, Inc., in San Francisco

## Dr Axel Hoos (Philadelphia, U.S.A.)

Non-Executive Director

- Currently Senior Vice President Oncology R&D at GlaxoSmithKline
- Previously Clinical Lead on Ipilimumab at Bristol-Myers Squibb
- Co-Director of the think-tank Cancer Immunotherapy Consortium

## Paul Hopper (Sydney, Australia)

Executive Chairman

- International & ASX biotech capital markets experience particularly in immuno-oncology & vaccines
- Chairman of Viralytics, Founder & Director of Prescient, Founder of Imugene & Polynoma LLC, former Director pSivida, Somnomed & Fibrocell Science

## Prof Ursula Wiedermann (Vienna, Austria)

Chief Scientific Officer

- Co-inventor of HER-Vaxx;
- Professor of Vaccinology at Medical University of Vienna

## Prof Christoph Zieliniski (Vienna, Austria)

Head of Scientific Advisory Board

- Chairman of the Comprehensive Cancer Centre in Vienna
- Chairman of the Centre for Eastern EU Organisation for Research and the Treatment of Cancer (CEEORTC)
- Editor in Chief and President Nominee of European Society of Medical Oncology (ESMO)

## Dr Nick Ede (Melbourne, Australia)

Chief Technology Officer

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

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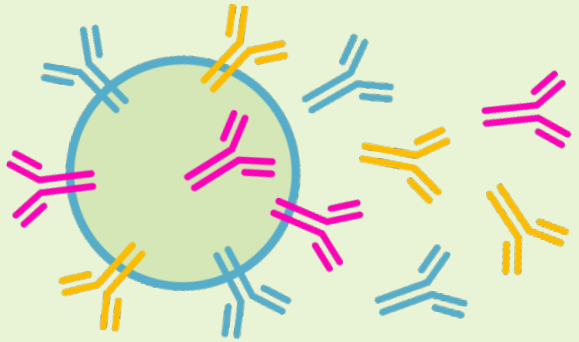
# A BETTER WAY TO MAKE ANTIBODIES TO TREAT CANCER?

## IN A FACILITY

For example, Roche's Herceptin

VS

## USING B CELLS IN YOUR OWN BODY



Teaching B cells to make antibodies using peptide mimotopes

**B Cells** are cells in the human body that naturally produce millions of antibodies

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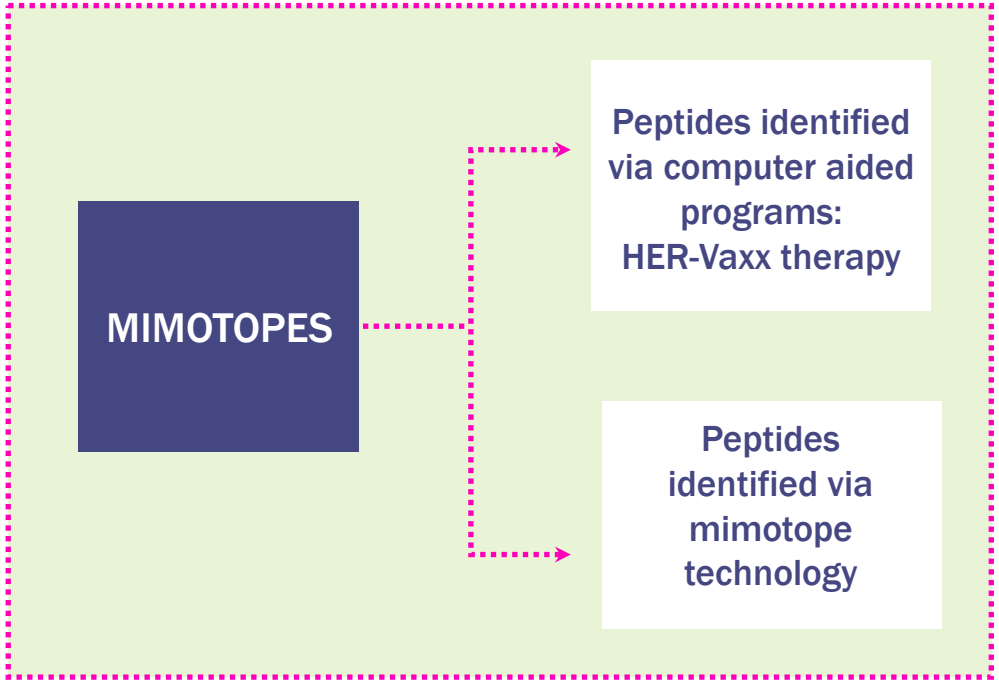
# NOVEL MIMOTOPE PEPTIDE PROGRAMS

- A mimotope is a small molecule, often a peptide, which mirrors the structure of an epitope, the specific target an antibody binds to.
- Because of this property, the mimotope induces an antibody response similar to the one elicited by the epitope.
- A mimotope causes your B cells to produce an antibody copy of the antibody you want to “mimic”
- Potential tool for selecting novel vaccine candidates against a variety of tumors
- Technology can be used to copy any approved antibody on the market today



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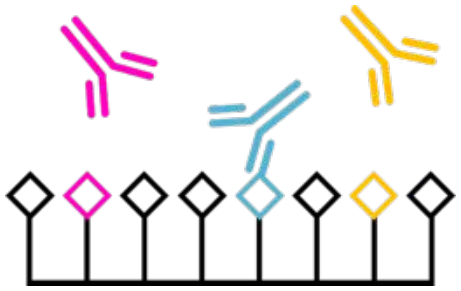
# MIMOTOPE: PLATFORM TECHNOLOGY

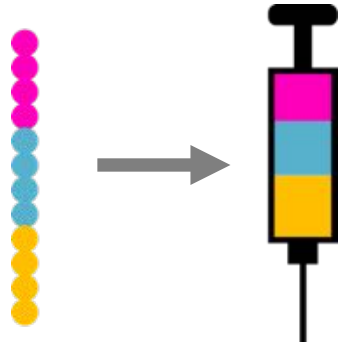
## SELECTION OF MIMOTOPES

A library of mimotopes can be interrogated with any monoclonal antibody to identify the mimotopes to which it binds



## CREATION OF A VACCINE

The selected mimotope or mimotopes can be used in isolation or combination to create a B-cell peptide therapy with the appropriate carrier system and adjuvant.

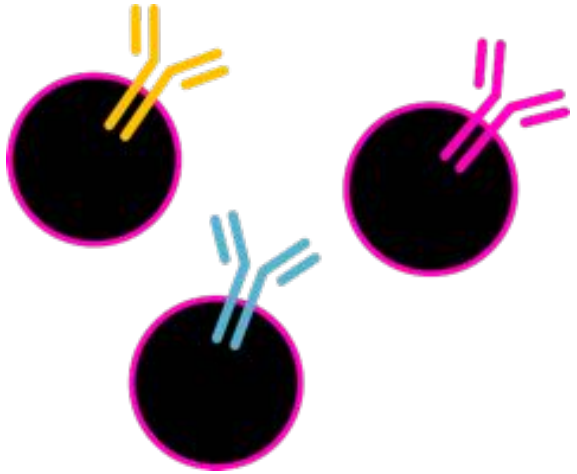


## IMMUNIZATION

Immunization with the peptide will lead to the patients B-cells producing copies of the Ab you want to mimic

## ENDOGENOUS AB PRODUCTION

Successful delivery will result in endogenous Ab production with associated immune memory



**The mimotope platform has the potential to be part of the next wave of immuno-oncology products. It makes multi-level therapies against a combination of targets achievable.**

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# ADVANTAGES OF MIMOTOPE INDUCED B-CELL BASED ANTIBODIES V. SYNTHETIC ANTIBODIES

| Issue | Natural B Cell Derived Antibodies | Monoclonal Antibodies |
|---|---|---|
| Safety | Stimulates the immune system to produce natural Abs, potentially safer, as demonstrated by HER-Vaxx | 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 - single shot |
| Durability | Antibodies continuously produced a lasting immune response to inhibit tumor recurrence | Half life up to 12 days sometimes less |
| Usability | Potentially low numbers of vaccinations required per year | Requires regular infusion |
| Cost | Low cost of production enables greater pricing flexibility facilitating combinations and opening up additional markets | Expensive course of treatment >USD100K per year in the US |

**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.**

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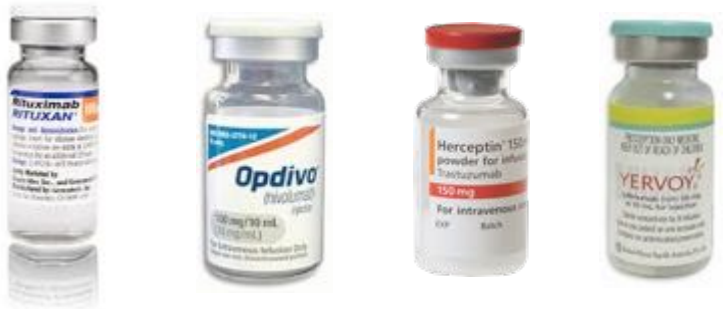
# THE MONOCLONAL ANTIBODY (mAb) MARKET

- Multiple antibody therapies are approved to treat cancer, for example:

**Sales in 2016**

- **Herceptin:** >US$6.7 billion
- **Perjeta:** >US$1.8 billion
- **Rituxan:** >US$7.3 billion
- **YERVOY®:** >US$1.0 billion
- **OPDIVO®:** >US$3.7 billion
- **KEYTRUDA:** >US$1.4 billion




**Total monoclonal antibody market is currently at US$60 billion**

- <u>All of these antibodies are manufactured in a facility.</u>

- Instead of infusing patients with antibodies synthesized in a factory, what if we can induce the patient's own B-cells to make similar cancer-fighting antibodies using Imugene's mimotope technology?

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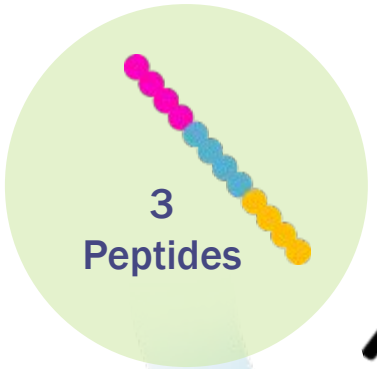
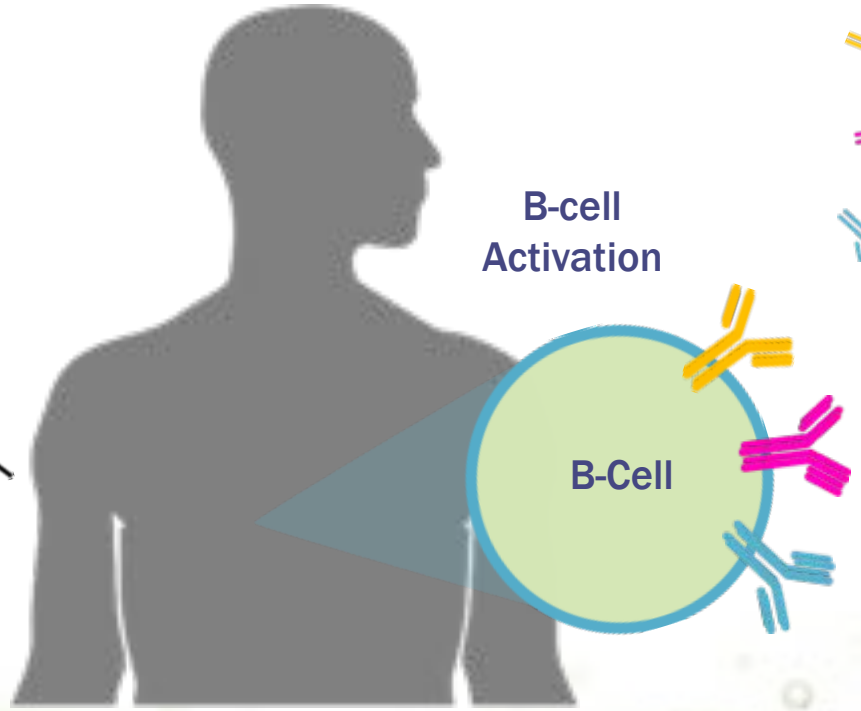
# HER-Vaxx MIMOTOPE: MECHANISM OF ACTION

**Peptides**
"mimic" the epitope



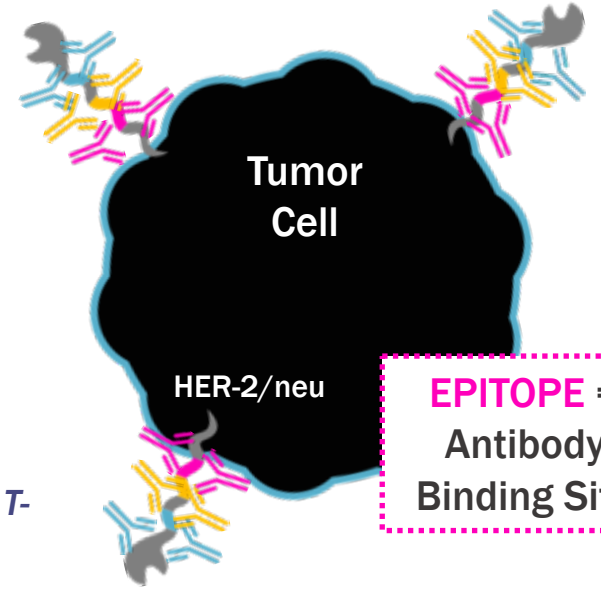

HER-Vaxx Immunotherapy




B-cell Activation

HER-Vaxx Antibody Secretion

*Via helper T-cells*




**EPITOPE** = Antibody Binding Site


HER-Vaxx attacks the same target as the the world's largest selling breast cancer drug Herceptin

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# HER-Vaxx IS A PHASE 1B/2 STAGE MIMOTOPE PEPTIDE THERAPY BEING DEVELOPED FOR HER2+ GASTRIC CANCER

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# PHASE 1 IN BREAST CANCER, COMPLETED AT MEDICAL UNIVERSITY OF VIENNA- SINGLE AGENT, NO CHEMO

## DESIGN

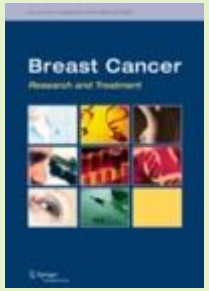
- 10 patients
- All late stage breast cancer patients
- HER-2 +/++
- Life expectancy > 4 months
- Conducted at Medical University of Vienna

## *RESULTS

- Patients developed anti-HER-2 antibodies
- Induction of cytokines (Th1 biased; IFNγ)
- 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
- Reviewed in peer publication

## CLINICAL ENDPOINTS

1. **Safety and Tolerability**
2. **Immunogenicity: antibodies and cellular responses**



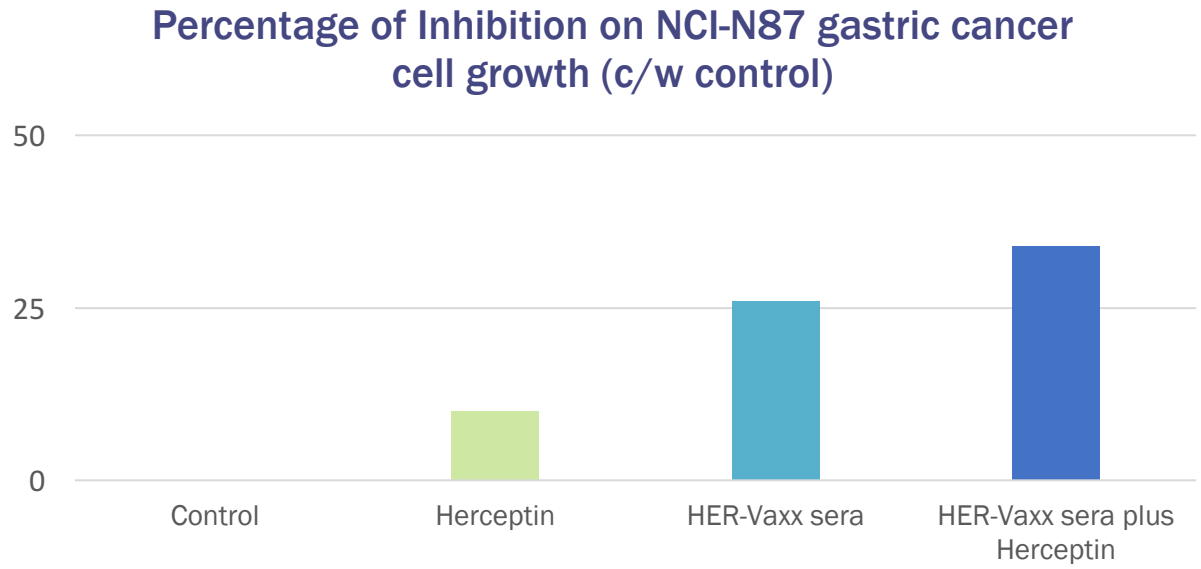

* Wiedermann et. al., Breast Cancer Res Treat. 2010 Feb;119(3):673-83.

**Safety, Efficacy, Durability, Usability, Cost**

* Data Available in Science Booklet

# HER-VAXX INHIBITS HER-2 EXPRESSING CELLS

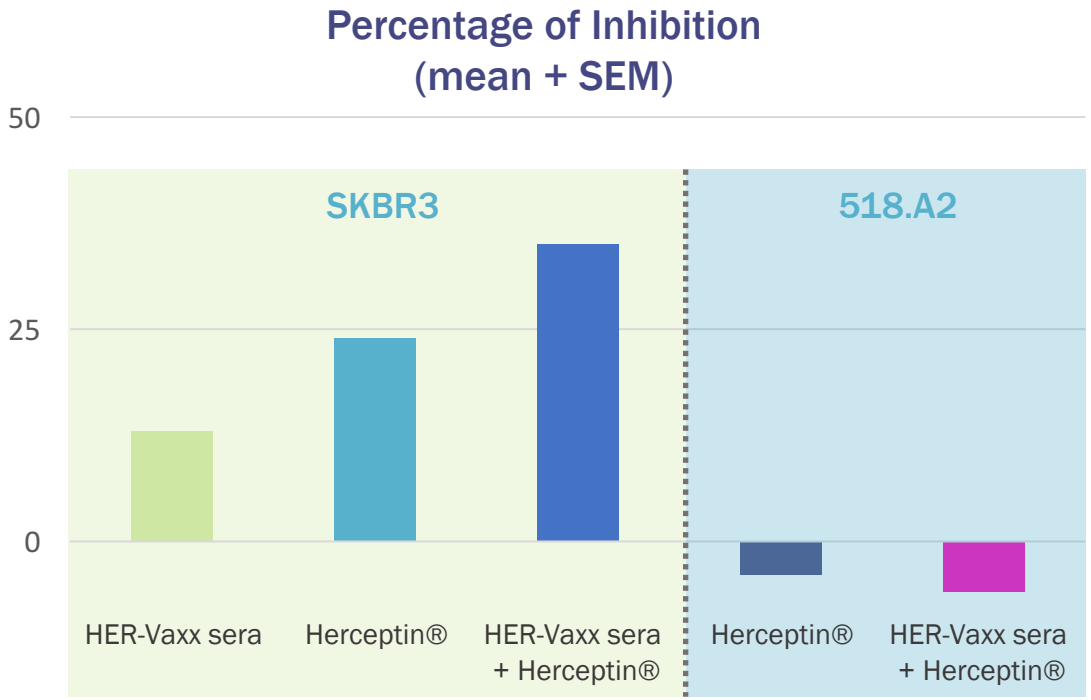
**HER-Vaxx antibodies demonstrate anti-tumour effect by inhibiting validated HER-2+ gastric cell line**




HER-2+ gastric cancer cells*

*Collaboration with US company 2017

**Combination with Herceptin shows significantly higher inhibition than Herceptin alone.**




HER-2+ breast cancer cells*

*BMC Cancer2017, Wiedermann Feb. 2017

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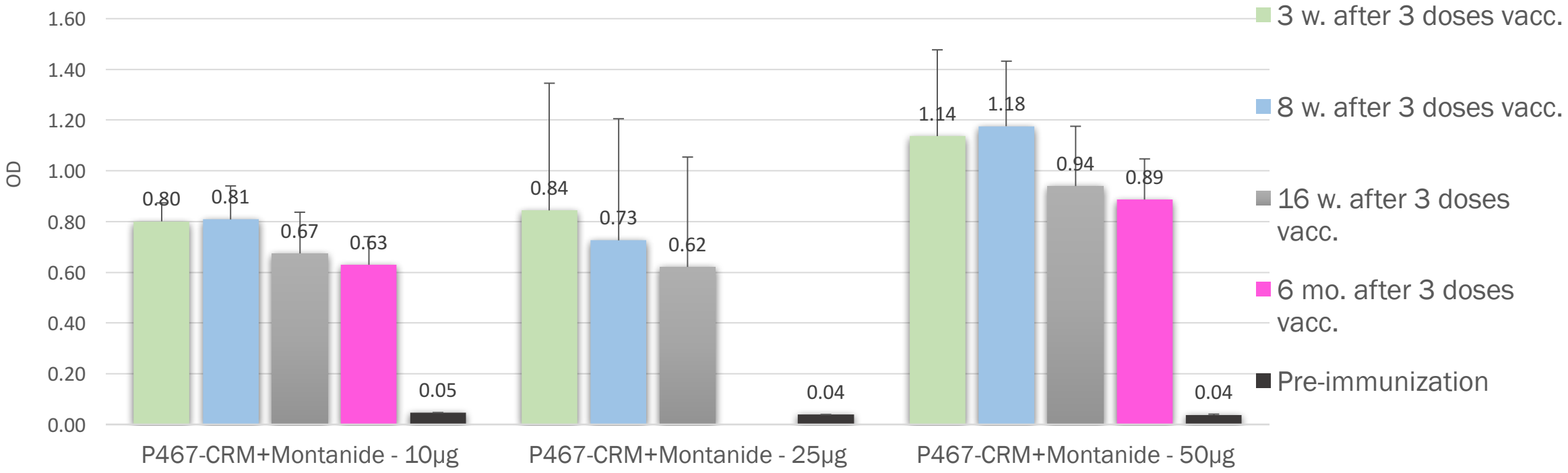
# PHASE 1B/2 ENHANCED GASTRIC FORMULATION

## Her-2/neu specific IgG kinetic, after last immunization




**In the mouse model the new formulation sees circulating antibodies maintained for 6 months which equates to many years in humans.**

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# PHASE 1B/2, IN GASTRIC CANCER

## Phase 1b lead-in

- Open label
- ~Up to 18 patients in 3 cohorts of up to 6 pts per cohort
- Combination with chemo/cisplatin
- Endpoints:
  - Recommended Phase 2 Dose of HER-Vaxx
  - Safety: any HER-Vaxx toxicity
  - Immunogenicity (anti-HER-2 antibody titres)

## Phase 2

- Open label
- ~70 patients from sites in Asia
- Combination with chemo
- Randomized
- Primary Endpoints:
  - TBD PFS and/or OS
  - (cont. on Ph1b results)
- Secondary endpoint:
  - Immune response

**2H, 2017 : Patients Enrolled**

**1H, 2018: Early Patient Data Available**

**1H, 2018: Interim Ph1b Patient Data Available**

**2H, 2018: Final Ph1b Patient Data Available**

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# OUR INVESTIGATORS AND STUDY CENTERS

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# GASTRIC MARKET OPPORTUNITY

- Asia is the largest market for gastric cancer globally
- Gastric cancer is the second leading cause of cancer mortality in the world & its management, especially in advanced stages, has evolved relatively little
- ~1 million gastric cancer cases per year; ~19% patients with metastatic gastric cancer are HER-2 positive
- Surgery, chemotherapy, radiation & Herceptin are the key treatments
- In many countries, particularly Asia, chemotherapy such as capecitibine and 5-FU, is the standard of care, not Herceptin


Chemotherapy


Monoclonal antibody

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# MARKET OPPORTUNITY

| Indications | Gastric Cancer | Breast Cancer |
|---|---|---|
| Incidence | 1 million cases of newly diagnosed cases, ~190k are HER2+* | 1.67m cases of newly diagnosed cases; ~418k are HER2+* |
| Prognosis | Poor. Median survival is 7-10 months | Varies in breast cancer type. 0.5m deaths per year |
| % of Patients HER2+ prevalence | ~19% | ~25% |
| Herceptin® cost | ~3,500 per dose every 3 weeks = $60,000 per year | ~3,500 per dose every 1-2 weeks = 91,000-182,000 |
| Herceptin® benefits (in conjunction with surgery and chemotherapy) | 2.7 months OS (overall survival) improvement than chemo alone | Improves OS by 33%-52%. Varies with breast cancer type and line of disease. |

*http://globocan.iarc.fr/old/FactSheets/

- **2017** Herceptin® sales total 6.7b in gastric and breast cancer
- Gastric cancer treatment market to grow at the rate of 14.6% annually to $4.4 billion by 2024; **The Asia-Pacific gastric cancer market is set to grow from its 2015 value of $1.3 billion to $2.7 billion by 2022**
- **HER-Vaxx** could address not only relapsed patients, but patients in all stages of cancer progression.
- **HER-Vaxx** could **have a significantly more convenient dosing regime** over Herceptin®'s weekly and lengthy infusions.



*https://www.thepharmaletter.com/article/gastric-cancer-treatment-market-to-grow-at-the-rate-of-14-6-annually-to-4-4-billion-by-2024-globaldata

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# IMUGENE PIPELINE

| HER-Vaxx (IMU-131) | | Discovery | Pre-Clinical | Phase IB | Phase 2 |
|---|---|---|---|---|---|
| Open Label Randomized, Controlled Study in Gastric Cancer | Chemotherapy + or - HER-Vaxx | | | | |
| *Combination Study in breast cancer | HER-Vaxx + Herceptin | | | ▲ | |
| *Herceptin Resistant/Failed Study | HER-Vaxx + Chemotherapy | | | ▲ | |
| *HER2+ in bladder and ovarian, NSCLC etc. | HER-Vaxx + Chemotherapy | | | ▲ | |

*(IST) Investigator Sponsored or Collaboration study
*Christoph Zieliniski, CECOG President, ESMO president nominee, engaged

▲ = Initiated upon RP2D

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# MIMOTOPE B-CELL PEPTIDE THERAPY

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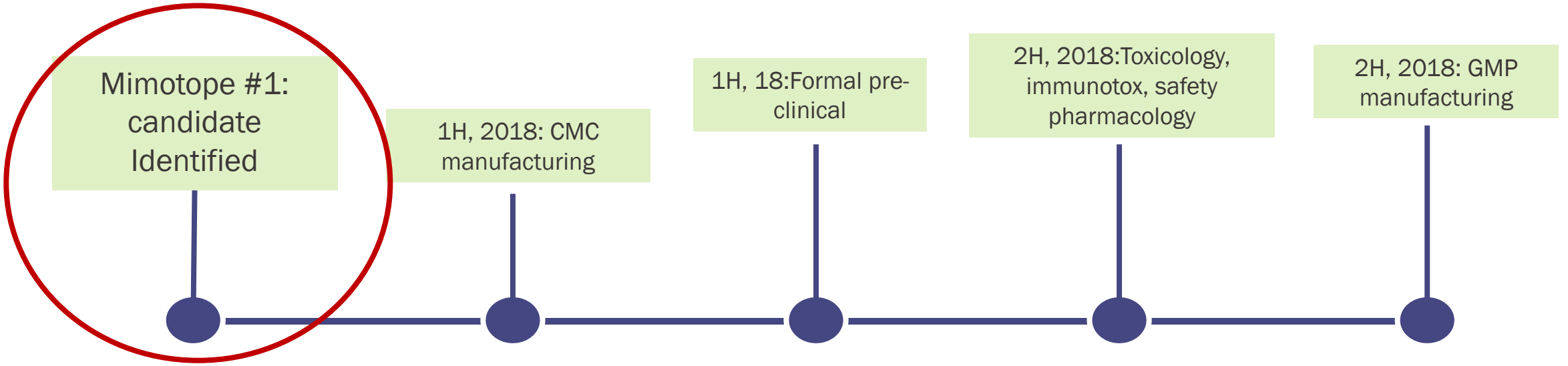
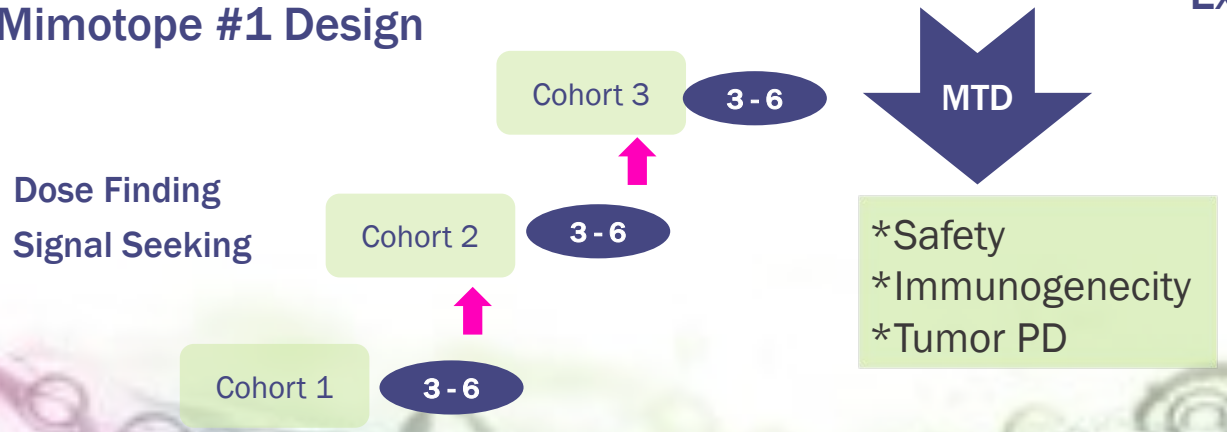
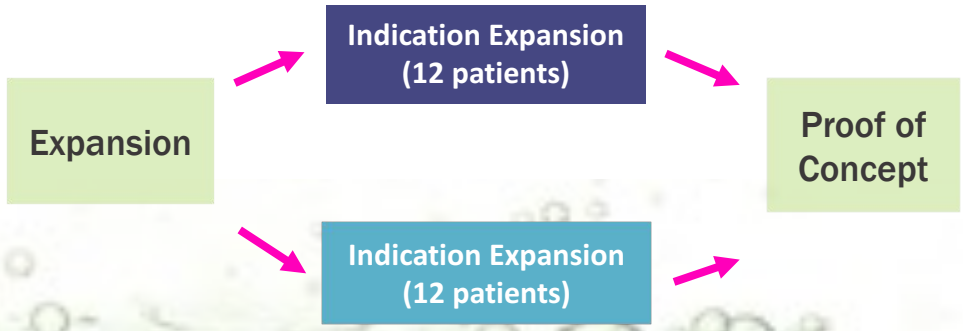
# MIMOTOPE PROPOSED DEVELOPMENT PATH 2017-2018




## Proposed Phase I Mimotope #1 Design




## Expansions Assumption



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# IMUGENE DISCOVERY PIPELINE

| PROGRAM | MIMOTOPE IDENTIFICATION | IMMUNE CHARACTERIZATION | ID OF CANDIDATE | PRE-IND WORK | CLINICAL DEVELOPMENT |
|---|---|---|---|---|---|
| HER-Vaxx /Her2 Combo | → | | | | |
| *Mimotope #2 | → | → | → | | |
| *Mimotope #3 | → | | | | |
| Her2 / *Mimotope Combo | → | | | | |
| Combo #3? | TBD | | | | |

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# FINANCIAL SUMMARY

## ASX:IMU

| Market Cap (28/Dec/17) | $42.8M AUD, $33.3M USD |
|---|---|
| Ordinary Shares | 2.855 billion |
| 12 month price range | 1.2 cents – 2.8 cents AUD |
| Avg daily volume | 6.9M shares (September-December 2017) |
| Investment to Date | ~$22.4 m (public)<br>~$ 5.5 m (VC) |
| Cash & Equivalents | $11.9M as of December 2017 |

## Top 5 shareholders (as at Dec. 2017)

| | No. of Shares | % Capital |
|---|---|---|
| Platinum Asset Management | 276,874,515 | 9.70% |
| National Nominees Limited | 125,895,033 | 4.41% |
| Paul Hopper Executive Chairman | 71,696,875 | 2.51% |
| Merrill Lynch (Australia) Nominees Pty Limited | 62,347,506 | 2.18% |
| Sarah Cameron | 51,817,073 | 1.82% |

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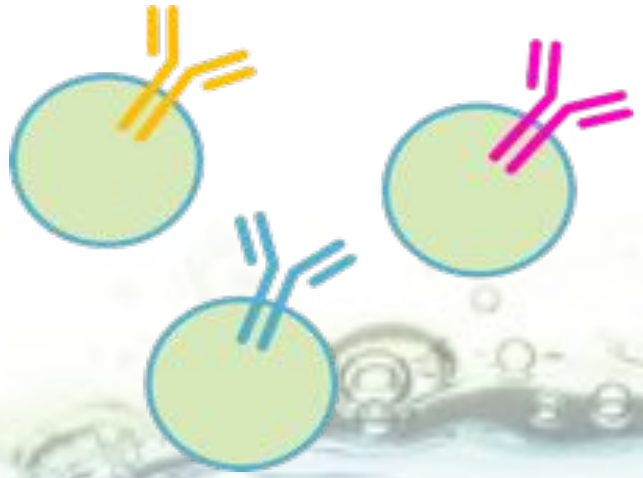

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# APPENDIX

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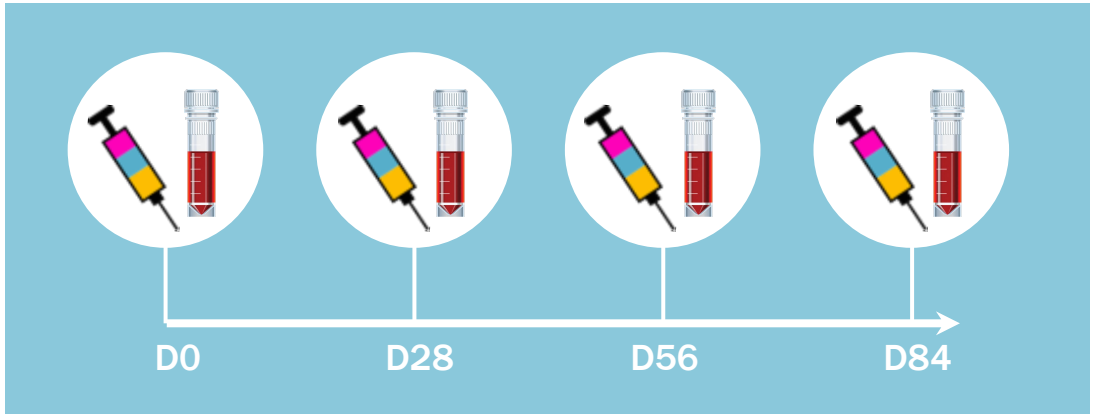
# PHASE IA STUDY DESIGN*

## ADMINISTRATION & READOUT SCHEDULE




Vaccination with 10µg of each peptide antigen

Blood draw

**Patient inclusion criteria**

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

**Primary endpoint**

- Safety & Tolerability

**Secondary endpoint**

- Immunogenicity
  - Specific antibodies
  - Cellular responses

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

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# PATIENT CHARACTERISTICS – AGES 55-84 *

| Patient ID | Age | Metastatic 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.

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# 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.

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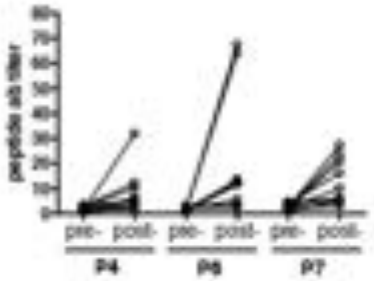
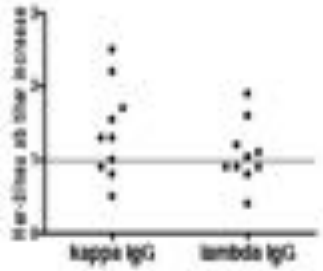
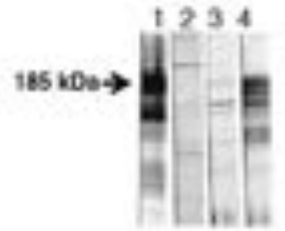
# PHASE 1 SECONDARY ENDPOINT – IMMUNOLOGIC RESPONSES

## ANTIBODY RESPONSES

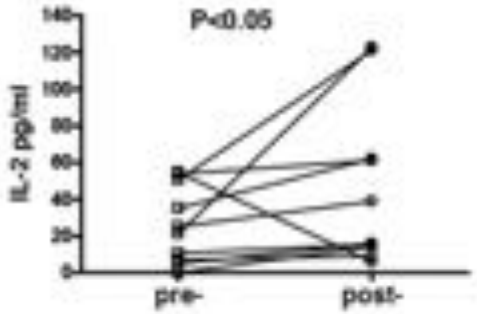


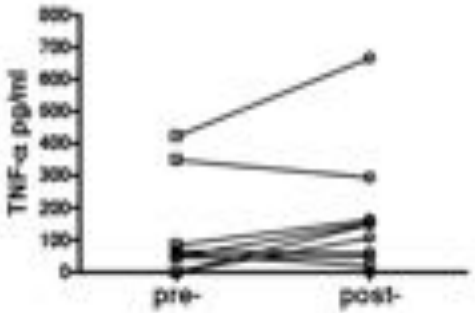



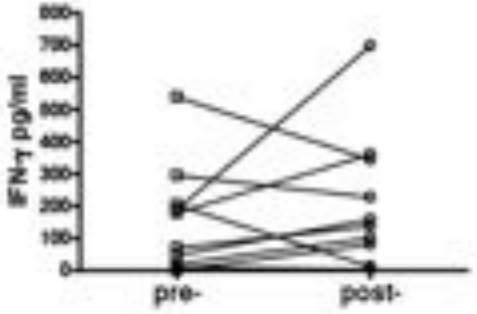




**Western blot analysis demonstrating increase of Her-2/neu-specific IgG post- vaccination in patient:**
(lane 1) Polyclonal rabbit anti Her-2/neu antibody was used as positive control
(lane 2) serum of a healthy volunteer as negative control
(lane 3) Serum prior
(lane 4) after completed vaccinations

## CELLULAR RESPONSES SHOW TH1 PROFILE




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

- 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)

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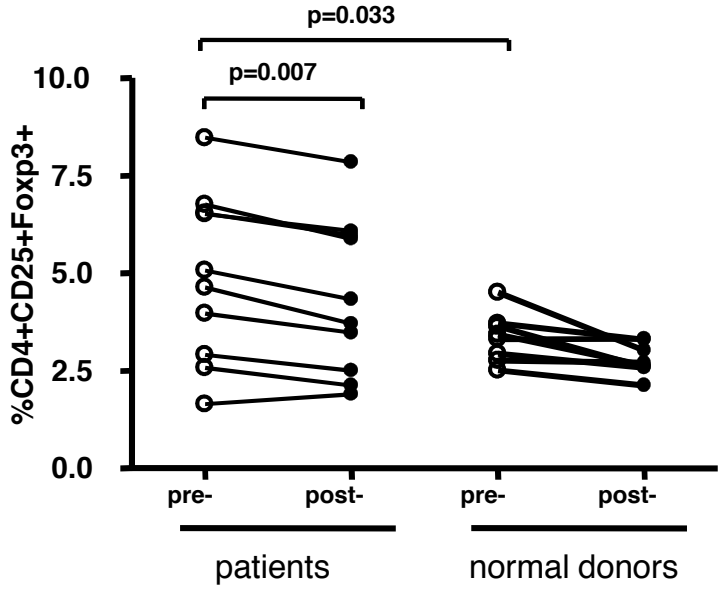
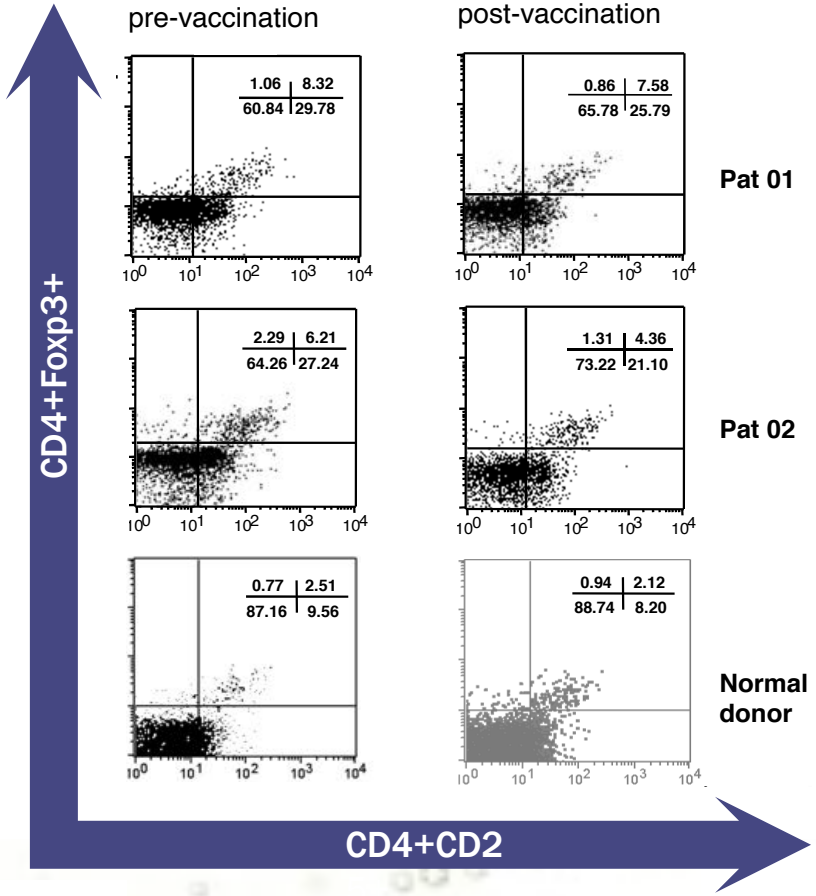
# REDUCTION IN REGULATORY T CELLS*




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

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# ENCOURAGING IMMUNOGENICITY, EVEN AT LOW DOSE, AND IN PATIENTS AGES UP TO 84 YEARS, WITH NO CARDIOTOXICITY

## Antibody and cellular responses in human

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

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

- 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

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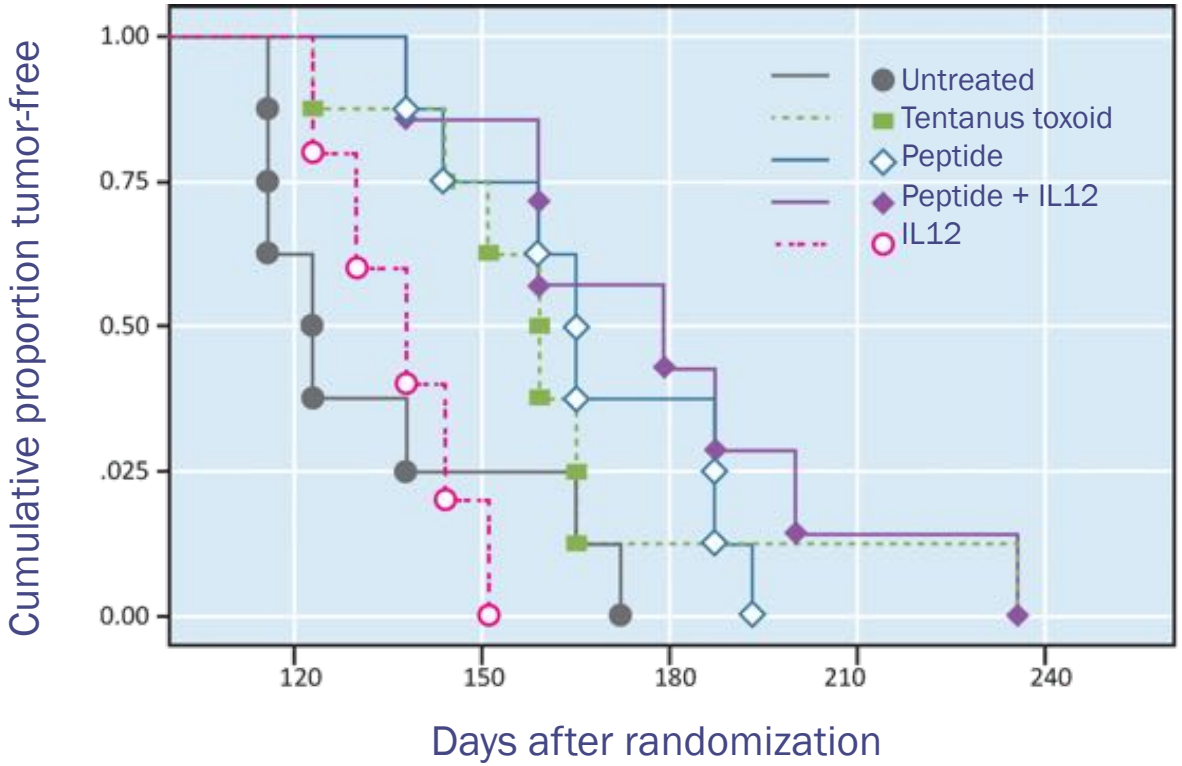
# TUMOR GROWTH INHIBITION IN VIVO*

## Time to disease progression




- 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

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**Preclinical study with tetanus toxoid–conjugated peptide antigens**

d 170 ⟷ d 65 ⟷ d 235

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# Leslie Chong

## Chief Executive Officer

leslie.chong@imugene.com

+61 458 040 433