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MIMOTOPE INDUCED B-CELL ANTIBODIES FOR IMMUNO-ONCOLOGY

Leslie Chong | Chief Executive Officer
2H/2017

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EXECUTIVE SUMMARY

- Experienced management & board
- Lead mimotope: HER-Vaxx Phase 1b/2 mimotope study in Her2+ gastric cancer (large unmet medical need by current existing therapies)
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- Discovery Pipeline: Mimotope candidate selection and Arginine modulators in pre-clinical development
- Numerous milestone announcements & valuation inflection points over next 12-18 months



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



Prof Ursula Wiedermann (Vienna, Austria)

Chief Scientific Officer

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



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

Non-Executive Director

- Currently 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



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



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



Dr Anthony Good (Sydney, Australia)

Clinical Program Manager

- Over 15 years oncology & immunology experience. Active in the development of Viagra, Revatio, Lipitor, Selzentry and Somavert.
- Ex Pfizer Global Research and Development

A BETTER WAY TO MAKE ANTIBODIES TO TREAT CANCER?

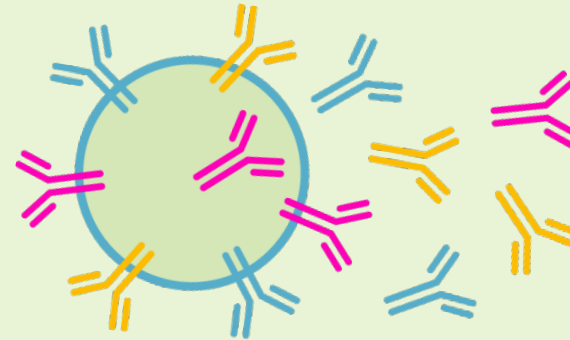
IN A FACILITY



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

MIMOTOPE: PLATFORM TECHNOLOGY

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”. This technology can be used to **copy any approved antibody** on the market today and is a tool for selecting novel vaccine candidates against a variety of indications.

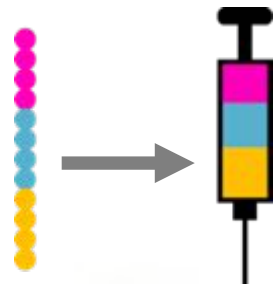
SELECTION OF MIMOTOPES

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 patient’s B-cells to produce 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 could produce multi-level therapies against a combination of targets.

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

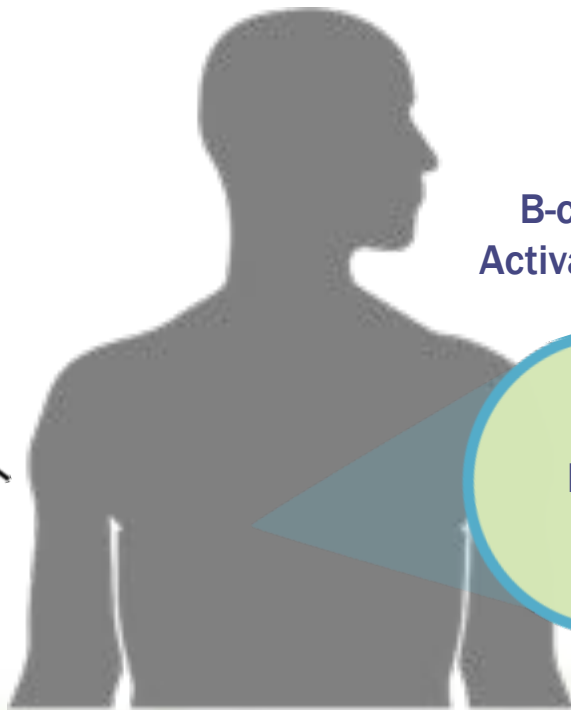
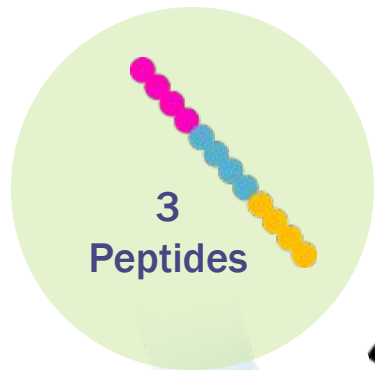


Total monoclonal antibody market is currently at US\$60 billion

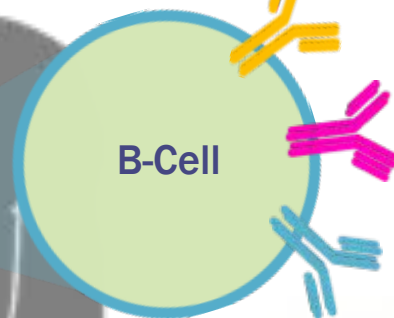
- All of these antibodies are manufactured in a facility.
- Instead of infusing patients with antibodies synthesized in a factory, what if we can induce the patient's own B-cells to make similar cancer-fighting antibodies using Imugene's mimotope technology?

HER-Vaxx MIMOTOPE: MECHANISM OF ACTION

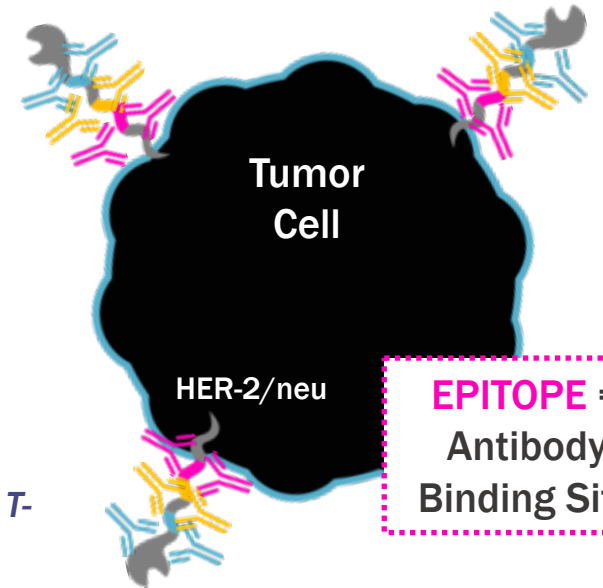
Peptides
"mimic" the
epitope



B-cell
Activation



HER-Vaxx
Antibody Secretion



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**

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; 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
- 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.

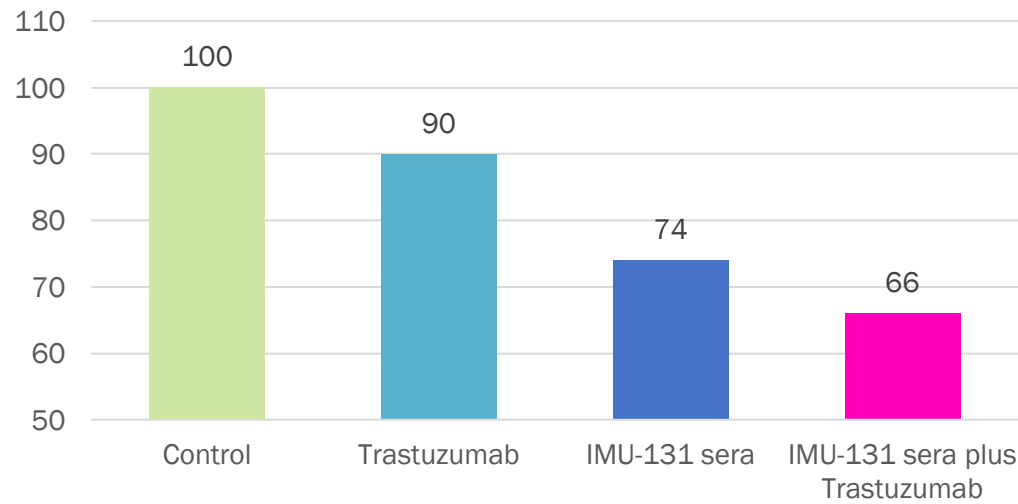
Safety, Efficacy, Durability, Usability, Cost

* 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

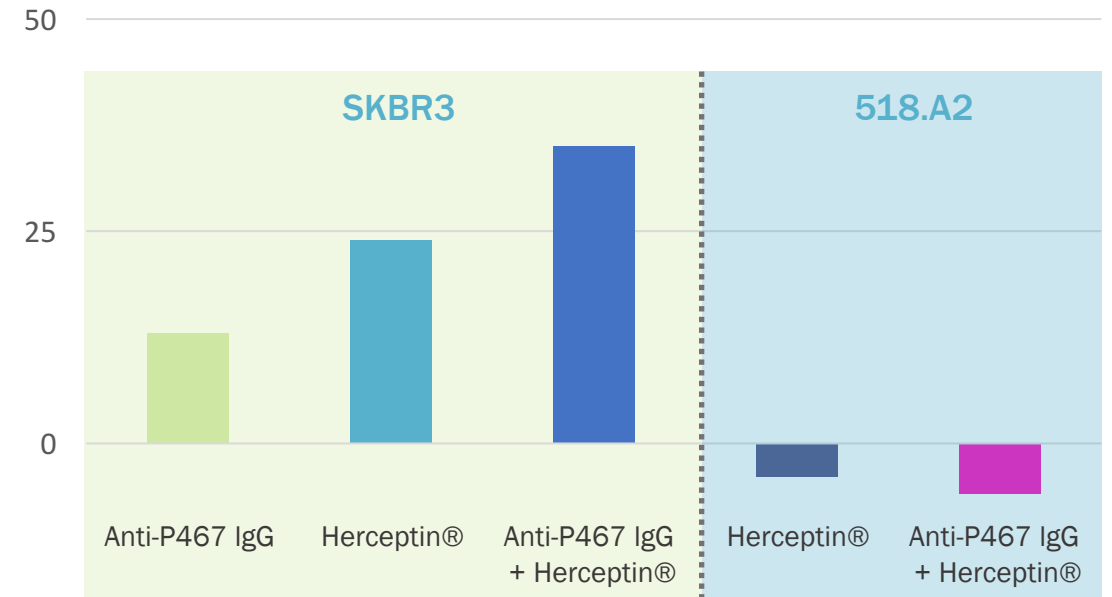
Effect of Trastuzumab and IMU-131 sera on NCI-N87 gastric cancer cell number (% of control)



HER-2+ gastric cancer cells

Combination with Herceptin shows significantly higher inhibition than Herceptin alone.

Percentage of Inhibition (mean + SEM)



HER-2+ breast cancer cells*

*BMC Cancer2017, Wiedermann Feb. 2017

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

2H, 2017: Early Patient
Data Available

2H, 2017: Interim Ph1b
Patient Data Available

1H, 2018: Final Ph1b
Patient Data Available



OUR INVESTIGATORS AND STUDY CENTERS



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 capecitabine and 5-FU, is the standard of care, not Herceptin



Chemotherapy



Monoclonal antibody

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.

- **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.**

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

*<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>

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	[Blue bar spanning Discovery, Pre-Clinical, and Phase IB]			[Grey bar spanning Phase 2]
*Combination Study in breast cancer	HER-Vaxx + Herceptin	[Blue bar spanning Discovery, Pre-Clinical, and Phase IB]			▲
*Herceptin Resistant/Failed Study	HER-Vaxx + Chemotherapy	[Blue bar in Discovery]	[Blue bar in Pre-Clinical]	▲	[Grey bar spanning Phase 2]
*HER2+ in bladder and ovarian, NSCLC etc.	HER-Vaxx + Chemotherapy	[Blue bar in Discovery]	[Blue bar in Pre-Clinical]	▲	[Grey bar spanning Phase 2]

*(IST) Investigator Sponsored or Collaboration study

*Christoph Zielinski, CECOG President, ESMO president nominee, engaged

▲ = Initiated upon RP2D

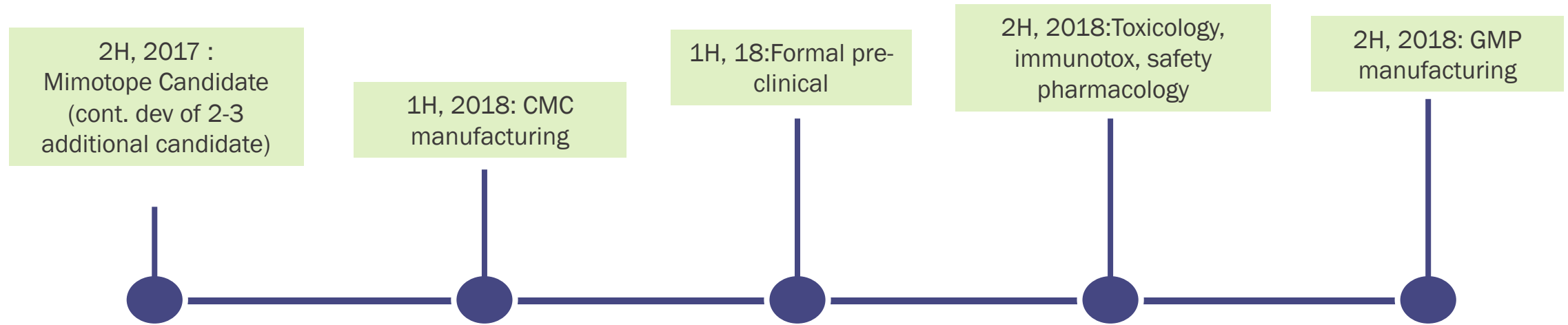
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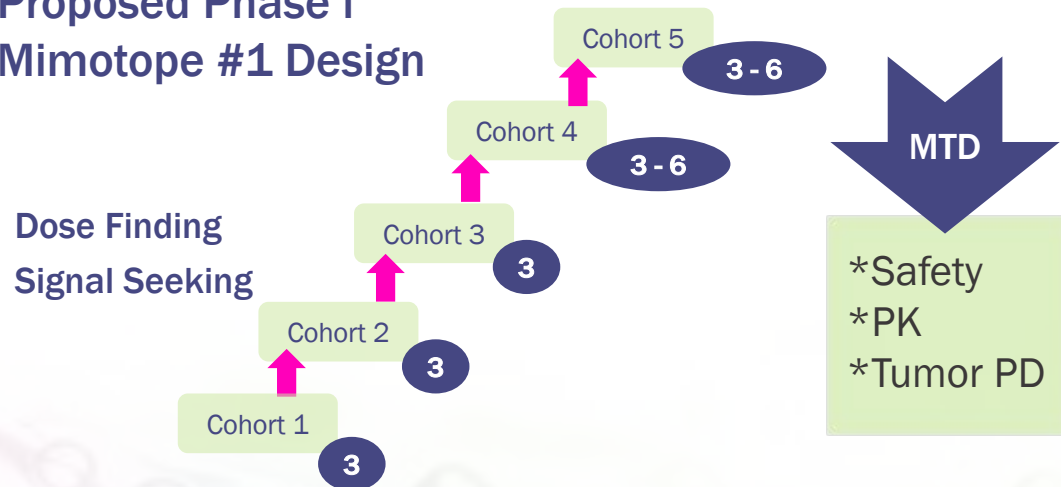


MIMOTOPE B-CELL PEPTIDE THERAPY

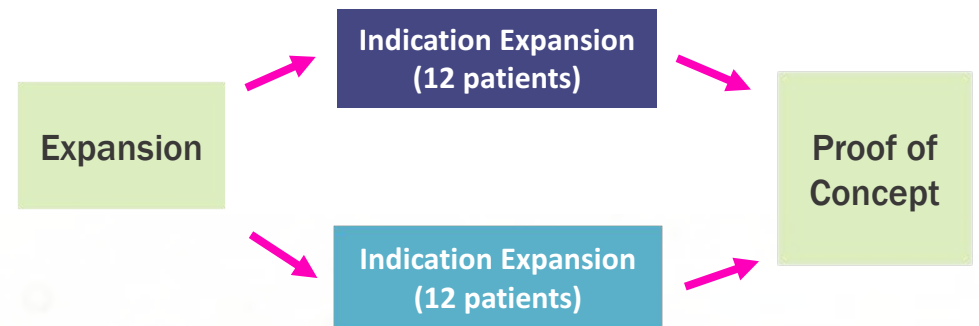
MIMOTOPE PROPOSED DEVELOPMENT PATH 2017-2018



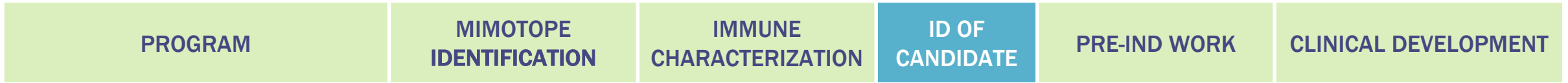
Proposed Phase I Mimotope #1 Design



Expansions Assumption



IMUGENE DISCOVERY PIPELINE



HER-Vaxx /Her2 Combo



*Mimotope #2



*Mimotope #3



Her2 / *Mimotope Combo



Combo #3?

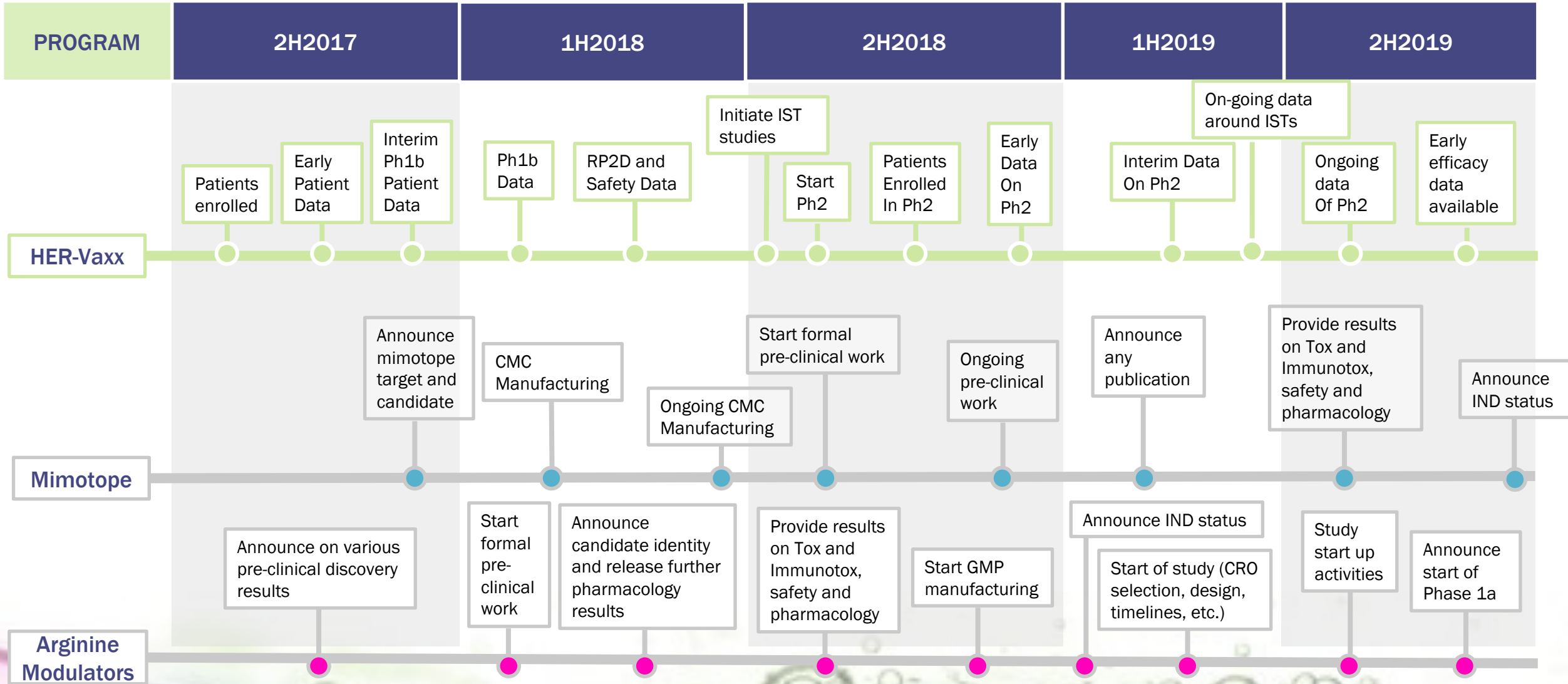
TBD



Arginine Modulator



MILESTONES AND DELIVERABLES



FINANCIAL SUMMARY

ASX:IMU

Market Cap (14/Jul/17)	\$33.1M AUD, \$25.7M USD
Ordinary Shares	2.365 billion
12 month price range	0.7 cents – 2.1 cents AUD
Avg daily volume	2M shares (April-June 2017)
Investment to Date	~\$15.2 m (public) ~\$ 5.5 m (VC)
Cash & Equivalents	\$4.8M as of July 2017

Top 5 shareholders (as at Sept. 2017)

	No. of Shares	% Capital
Platinum Asset Management	240,227,753	10.14%
National Nominees Limited	95,548,708	4.03%
Webinvest Pty Ltd	90,000,000	3.59%
Paul Hopper Executive Chairman	66,424,732	2.81%
Tisia Nominees	65,899,999	2.55%

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APPENDIX

SR. TEAM MEMBER ON
MARKETED ONCOLOGY
DRUGS



ZELBORAF[®]
(vemurafenib) tablets

CABOMETYX[™]
(cabozantinib) tablets
60 mg | 40 mg | 20 mg

TECENTRIQ[®]
atezolizumab INJECTION FOR
INTRAVENOUS USE 1200 mg

HERCEPTIN® (TRASTUZUMAB) MILD TREATMENT RELATED SIDE EFFECTS

- Diarrhea
- Redness or irritation at injection (IV) site
- Muscle/joint/back pain
- Stomach or abdominal pain
- Headache
- Sleep problems (insomnia)
- Nausea and vomiting (may be severe)
- Weight loss



HERCEPTIN® (TRASTUZUMAB)

SERIOUS TREATMENT RELATED SIDE EFFECTS – BLACK BOX WARNING¹

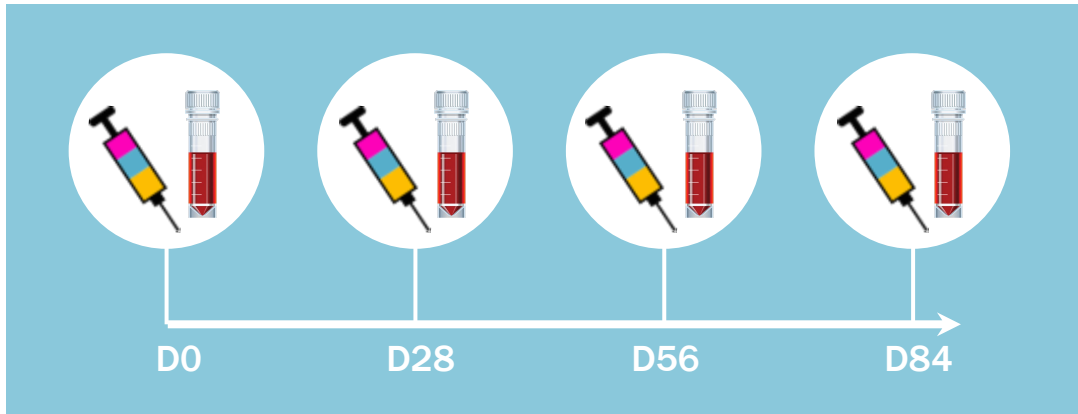
- **CARDIOMYOPATHY:** Herceptin can result in sub-clinical and clinical cardiac failure manifesting as CHF (congestive heart failure), and decreased LVEF (left ventricular ejection fraction).
- **INFUSION REACTIONS: PULMONARY TOXICITY:** Herceptin administration can result in serious and fatal infusion reactions and pulmonary toxicity.
- Anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome.



1. Herceptin Product Label – full prescribing information

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 expectancy > 4 mo

Primary endpoint

- Safety & Tolerability

Secondary endpoint

- Immunogenicity
 - Specific antibodies
 - Cellular responses

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

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.

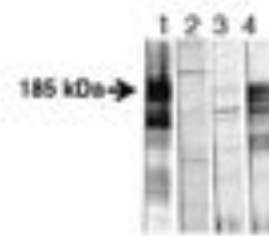
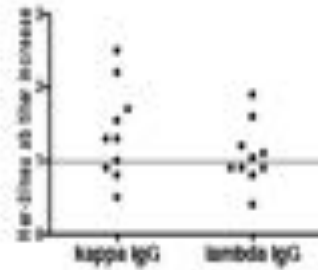
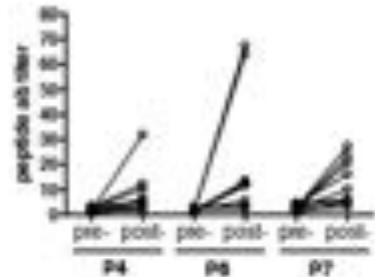
SAFETY AND TOLERABILITY – FEW GRADE 1 LOCAL REACTIONS, NONE SYSTEMIC*

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

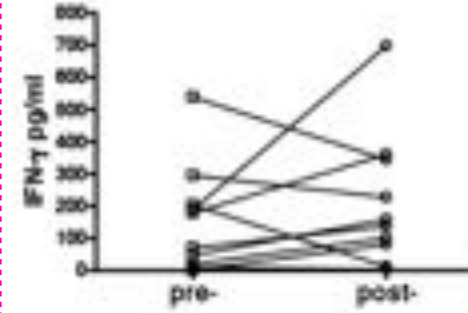
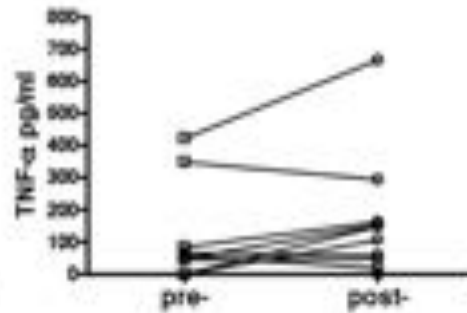
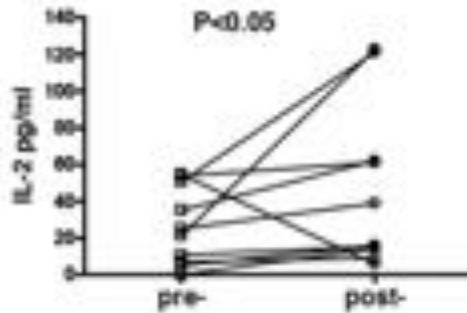
ANTIBODY RESPONSES



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

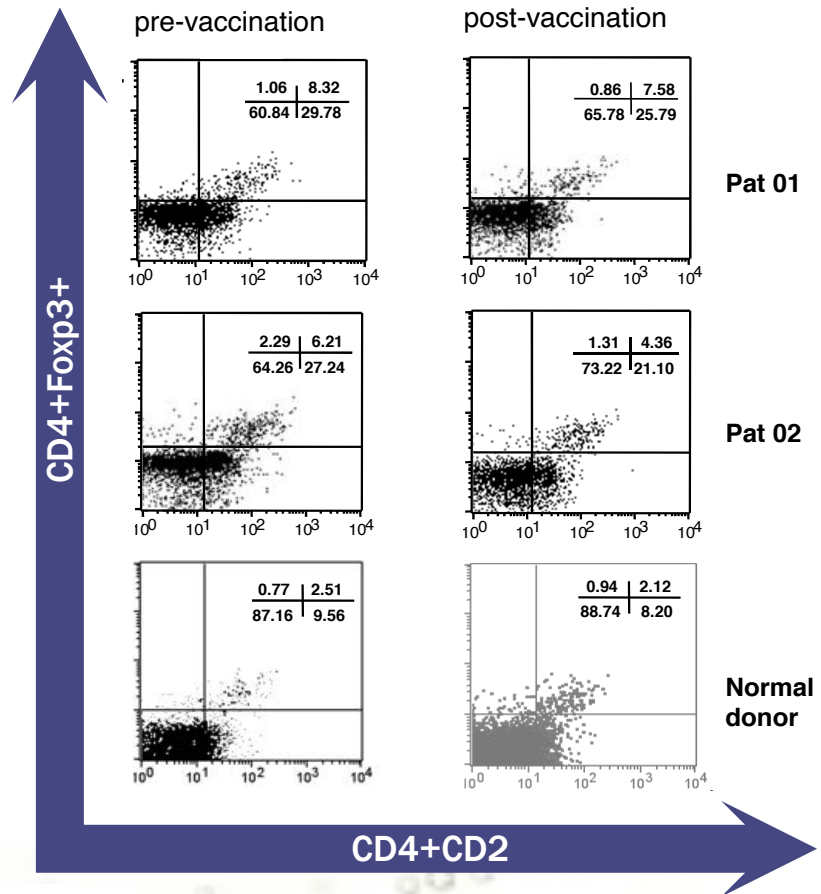
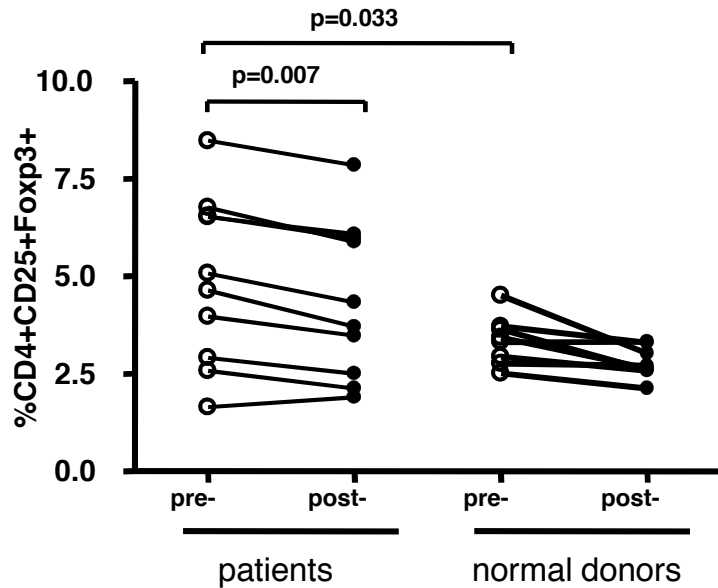
CELLULAR RESPONSES SHOW TH1 PROFILE



* 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)

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.

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, IFN γ , TNF	T reg
1	↑ ↑ ↑	↑	-	- - -	↓
2	↑ ↑ ↑	↑	↑	↑ ↑ ↑	↓
3	↑ ↑ ↑	↑ (+/-)	-	↑ - -	↓
4	↑ ↑ ↑	↑	↑	- ↑ ↑	↓
5	↑ ↑ ↑	↑	↑	↑ ↑ ↑	↓
6	- - -	-	-	↓ ↓ ↓	↓
7	↑ ↑ ↑	↑	↑	- - -	↓
8	↑ ↑ ↑	↑ (+/-)	↑	↑ ↑ -	↑
9	↑ +/- +/-	↑	↑	↑ ↑ ↑	↓
10	- - -	-	-	+/- ↓ +/-	↓

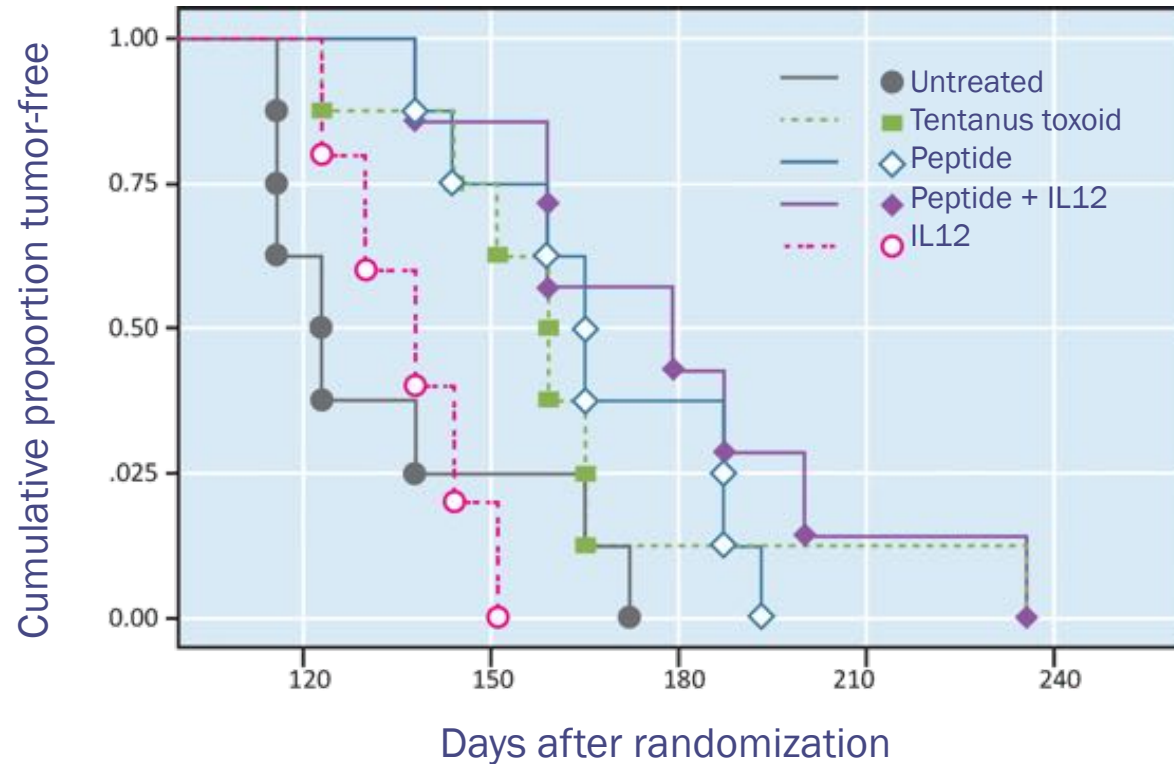
- Immunogenicity in 8/10 patients in Phase 1 study with 10 μ g of peptide antigen
- Good correlation with cellular responses (cytokines)
- Safe and well tolerated, in particular no cardiotoxicity
- Protective efficacy of peptides demonstrated in preclinical tumor model in mice showing delay of onset and reduced tumor growth

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

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

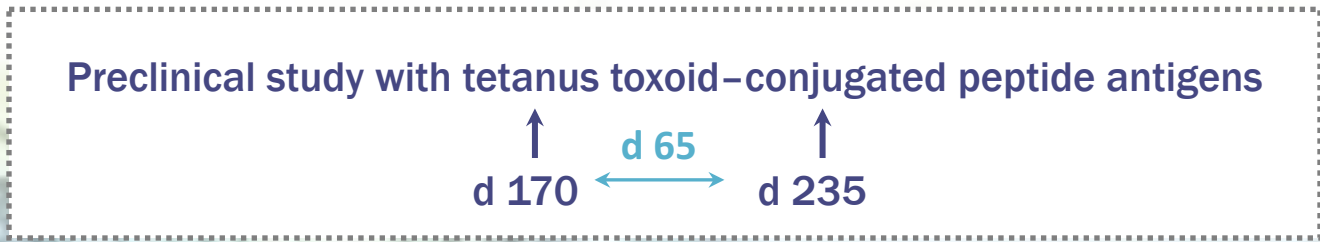
TUMOR GROWTH INHIBITION IN VIVO*

Time to disease progression

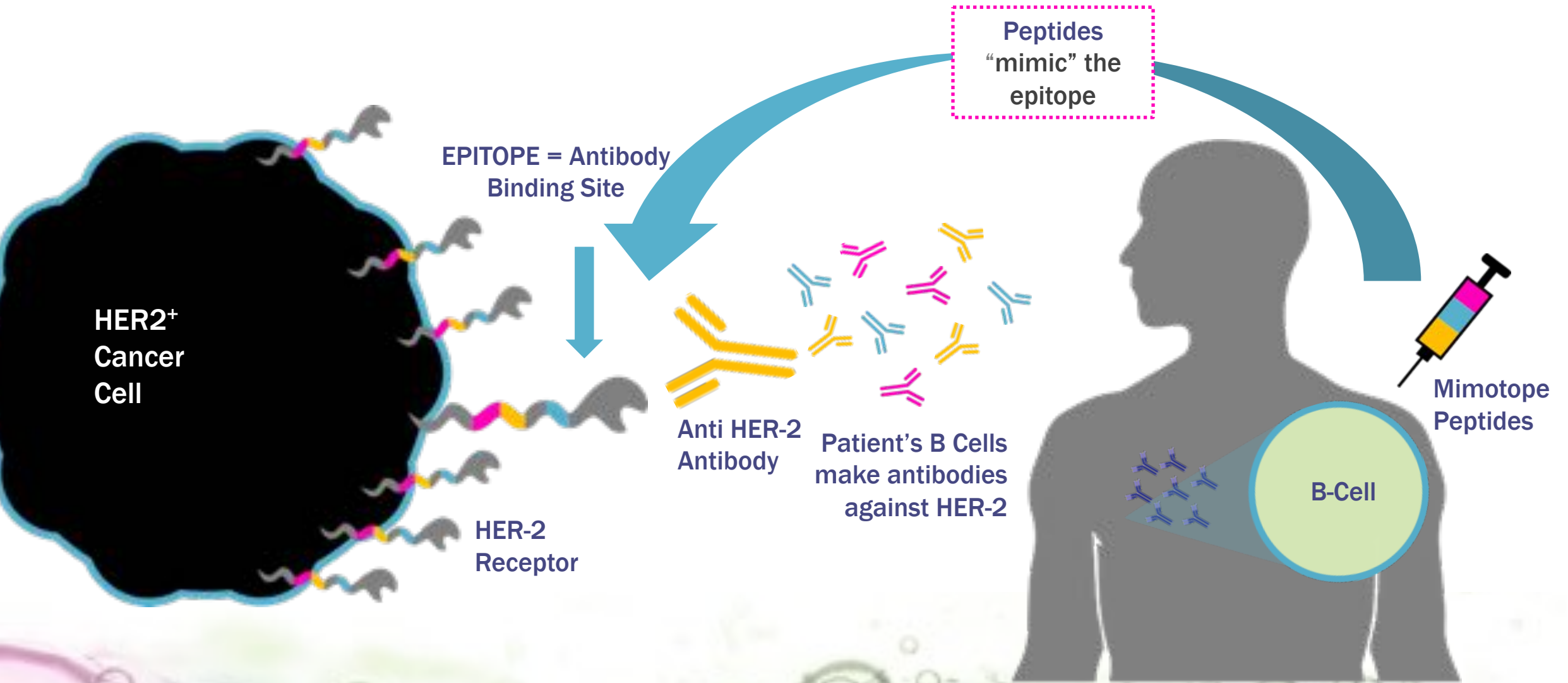


- Prolonged time to disease progression
- Immunization of c-neu transgenic mice (recognized HER2 cancer model) with tetanus toxoid-conjugated peptides P4, P6 and P7
- Vaccinated animals show significant delay in tumor onset and reduced growth kinetics
- Co-administration of IL-12 further improves the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

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

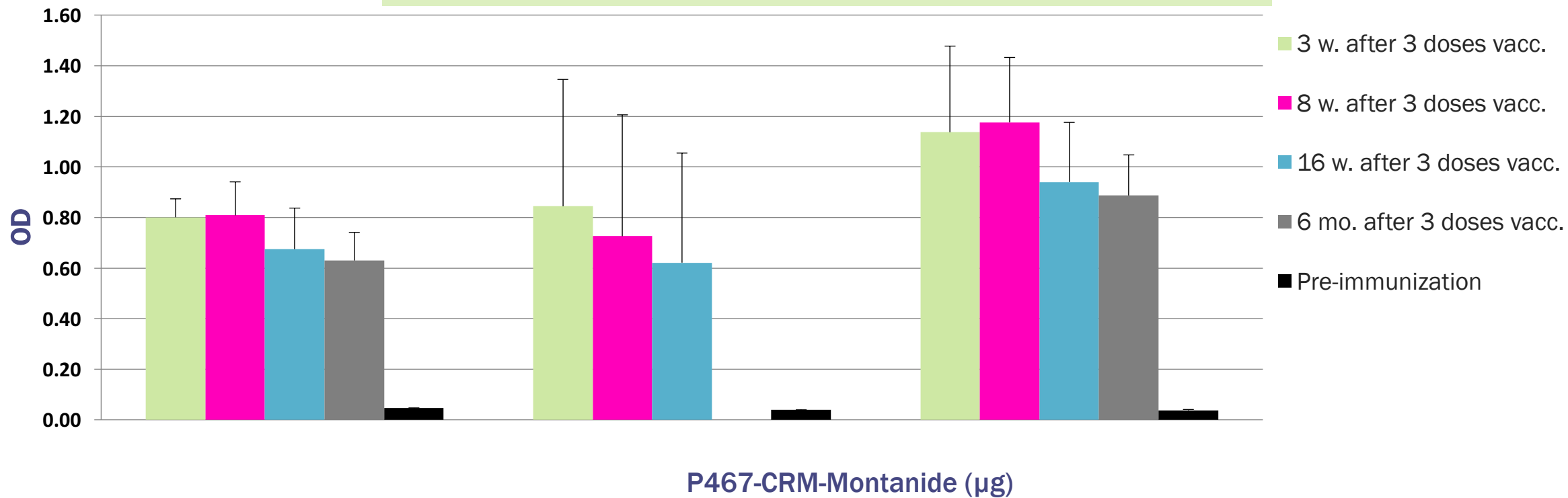


MIMOTOPE



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.

Leslie Chong

Chief Executive Officer

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