B Cell Based Antibodies for Immuno-Oncology

Leslie Chong
Chief Executive Officer
09-January-2017
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.
What Does Imugene Do?

We are developing cancer immunotherapy drugs based on antibodies.
IMU’s Value Proposition

✓ Promising science with impeccable provenance in the hottest area of cancer today – immuno oncology

✓ Broad Pipeline: HER-Vaxx & Mimotopes

✓ Breast Cancer clinical trial complete & on the cusp of recruitment on our second Phase 1b/2 clinical trial in gastric cancer

✓ Tight share register with leading Fund Manager, Platinum Asset Management

✓ Frequent, rich, quality news flow ahead

✓ Axel Hoos Sr. VP of immuno – oncology at GSK, plus team with successful track record in drug development

✓ Low market cap - undervalued against ASX peers
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
What is Cancer Immunotherapy?

• Immunotherapy is the treatment of cancer with substances or drugs that stimulate the patient’s immune response – known as active immunisation

• Unlike chemotherapy, immunotherapy drugs do not target the cancer directly

• Immunotherapy helps the patient’s own immune system recognise & attack cancer cells

• Typical immune responses are:
  – B Cells making antibodies to attack the cancer
  – T Cells developed by the thymus to attack the cancer
Two Compelling Antibody Programs and Commercial Opportunities

Imugene’s Pipeline B Cell Peptide technology

Peptides produced via computer aided programs: HER-Vaxx Vaccine

Peptides identified via mimotope technology

Building on the multi-levels of your own immune system

- Identification of cancer targets for variety of cancer indications
- Immune responses from conjugates and adjuvants
- B-Cell Peptide vaccines against checkpoint targets
What is an Antibody?  
A key Defense of the Immune System

**Antibodies** – Large Y-shaped protein. They are exquisitely made to attach themselves to a target sitting on an invading organism.

There are 2 ways to make antibodies

**In a factory**
For example, Roche’s Herceptin

**Using B cells in your own body**

**B Cells** – are like little antibody factories producing millions of antibodies against cancer targets
Advantages of B-Cell Based Antibodies

<table>
<thead>
<tr>
<th>Issue</th>
<th>B-Cell Immunotherapy</th>
<th>Monoclonal Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td>• Stimulates the immune system to produce natural Abs, potentially safer, as demonstrated by HER-Vaxx</td>
<td>• Synthetic Ab, with side effects (including ventricular dysfunction, CHF, anaphylaxis, immune mediation)</td>
</tr>
<tr>
<td>Efficacy</td>
<td>• Polyclonal Ab response reduces risk of resistance and potentially increases efficacy</td>
<td>• Monoclonal Ab - single shot</td>
</tr>
<tr>
<td>Durability</td>
<td>• Antibodies continuously produced a lasting immune response to inhibit tumor recurrence</td>
<td>• Half life up to 12 days sometimes less</td>
</tr>
<tr>
<td>Usability</td>
<td>• Potentially low numbers of vaccinations required per year</td>
<td>• Requires regular infusion</td>
</tr>
<tr>
<td>Cost</td>
<td>• Low cost of production enables greater pricing flexibility facilitating combinations and opening up additional markets</td>
<td>• Expensive course of treatment &gt;USD100K per year in the US</td>
</tr>
</tbody>
</table>

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.
A Mimotope Produces a Copy of an Antibody

• 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 it 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

• Greatly extends IMU’s oncology franchise and pipeline.

• Monoclonal antibody market currently at US$60bn annually

• December, 2016 progressed the mimotope platform with filing of 4 new patent applications
HER-Vaxx is a peptide vaccine being developed for HER2+ gastric cancer
HER-Vaxx: Mechanism of Action – How it Works

HER-Vaxx Immunotherapy

3 Peptides

B-cell Activation

HER-Vaxx

Antibody Secretion

Tumor Cell

HER-Vaxx attacks the same target as the world’s largest selling breast cancer drug Herceptin
Phase 1 in Breast Cancer, Completed at Medical University of Vienna

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

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

**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

HER-Vaxx Has Been Considerably Optimised Since Phase 1a

**First Generation**
- Three separate B Cell epitopes delivered in virosomes (used in Phase 1a).

**Second Generation**
- Incorporated the three B Cell epitopes into a single 49-mer peptide
- Greater than 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-Helper response), and added a montanide adjuvant
- Greater than 20x increase in antibody response *in vivo* (potentially extends patent life to 2036)
In the mouse model the new formulation sees circulating antibodies maintained for 6 months which equates to many years in humans.
Phase 1b/2, in Gastric Cancer

**Phase 1b lead-in**
- Open label
- ~18 patients in 3 cohorts of up to 6 pts per cohort
- Combination with chemo
- Endpoints:
  - Recommended Phase 2 Dose of HER-Vaxx
  - Safety: any HER-Vaxx toxicity
  - Immunogenicity (anti-HER-2 antibody titres)

**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

- **08-Nov, 2016:** Phase 1b/2 Commences
- **Q1, 2017:** Patient Enrolled
- **Q1-Q2, 2017:** Early Patient Data Available
- **Q3 2017:** Interim Ph1b Patient Data Available
- **Q4 2017:** Final Ph1b Patient Data Available
Huge Gastric Market Opportunity

• Gastric cancer is the second leading cause of cancer mortality in the world & its management, especially in advanced stages, has evolved relatively little
• ~20% 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
• Asia is the largest market for gastric cancer globally
## 2015 Big Pharma Antibody Deals

20% of the top 10 Big Pharma deals in 2015 were in the antibody space

### Top ten 2015 licensing transactions by announced total size

<table>
<thead>
<tr>
<th>Licensee</th>
<th>Licensor</th>
<th>Total Size (US $M)</th>
<th>Upfront (US $M)</th>
<th>Subject</th>
<th>Stage</th>
<th>Primary Rx Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sanofi</td>
<td>$4,266</td>
<td>$445</td>
<td>Sanofi to develop Hanmi’s Portfolio (specifically 3 assets) of long-acting diabetes treatment</td>
<td>Reformulation</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td>2</td>
<td>AstraZeneca</td>
<td>$4,090</td>
<td>$65</td>
<td>Discovery and development of antisense therapies for cardiovascular, metabolic and renal diseases</td>
<td>Discovery</td>
<td>Diversified</td>
</tr>
<tr>
<td>3</td>
<td>Vertex</td>
<td>$2,625</td>
<td>$75</td>
<td>Vertex and CRISPR to use CR1SPR-cas9 gene editing technology to discover and develop new treatment for genetic diseases</td>
<td>Discovery</td>
<td>Diversified</td>
</tr>
<tr>
<td>4</td>
<td>Gilead</td>
<td>$2,075</td>
<td>$300</td>
<td>Gilead Sciences to develop and commercialize Galapagos’ filgotinlb against rheumatoid arthritis</td>
<td>Phase II</td>
<td>Al/Inflam</td>
</tr>
<tr>
<td>5</td>
<td>Pfizer</td>
<td>$1,890</td>
<td>Undisclosed</td>
<td>Heptares and pfizer to develop novel drugs targeting GPCR against multiple therapeutic indications</td>
<td>Discovery</td>
<td>Diversified</td>
</tr>
<tr>
<td>6</td>
<td>BMS</td>
<td>$1,740</td>
<td>$350</td>
<td>BMS to develop and commercialize Five Prime’s CSFIR antibody program, including FPA-008 for immunology and oncology</td>
<td>Phase I</td>
<td>Diversified</td>
</tr>
<tr>
<td>7</td>
<td>Sanofi</td>
<td>$1,730</td>
<td>$300</td>
<td>Sanofi to develop and commercialize Lexicon’s sotagliflozin against diabetes, with an option to license</td>
<td>Phase III</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td>8</td>
<td>Amgen</td>
<td>$1,702</td>
<td>$45</td>
<td>Amgen to develop and commercialize Xencor’s bispecific cancer immunotherapy and inflammation programs</td>
<td>Preclinical</td>
<td>Diversified</td>
</tr>
<tr>
<td>9</td>
<td>Sanofi</td>
<td>$1,665</td>
<td>$640</td>
<td>PD-1 inhibitor and other new immuno-Oncology antibodies, with an option</td>
<td>Phase I</td>
<td>Cancer</td>
</tr>
<tr>
<td>10</td>
<td>Ultragenyx</td>
<td>$1,570</td>
<td>$10</td>
<td>Arcturus and Ultragenyx to discover and develop mRNA therapeutics using UNA Oligomer chemistry and LUNAR nanoparticle delivery platform</td>
<td>Discovery</td>
<td>Diversified</td>
</tr>
</tbody>
</table>
## What Could an IMU Deal Look Like?

### Top 20 Licenses with Upfront Payments > $50m

<table>
<thead>
<tr>
<th>Licensee</th>
<th>Licensor</th>
<th>Upfront ($M)</th>
<th>Equity ($M)</th>
<th>Stage</th>
<th>Rx Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi</td>
<td>Regeneron</td>
<td>$640</td>
<td></td>
<td>Phase I</td>
<td>Cancer</td>
</tr>
<tr>
<td>Celgene</td>
<td>Med Immune / AZ</td>
<td>$450</td>
<td></td>
<td>Phase III</td>
<td>Cancer</td>
</tr>
<tr>
<td>Sanofi</td>
<td>Hanmi</td>
<td>$445</td>
<td></td>
<td>Reformulation</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td><strong>Bristol-Myers Squibb</strong></td>
<td>Five Prime</td>
<td>$350</td>
<td></td>
<td>Phase I</td>
<td>Diversified</td>
</tr>
<tr>
<td>Astellas</td>
<td>Immunomic</td>
<td>$300</td>
<td></td>
<td>Discovery</td>
<td>Al/Inflam</td>
</tr>
<tr>
<td>Gilead</td>
<td>Galapagos</td>
<td>$300</td>
<td>$425</td>
<td>Phase II</td>
<td>Al/Inflam</td>
</tr>
<tr>
<td>Sanofi</td>
<td>Lexicon</td>
<td>$300</td>
<td></td>
<td>Phase III</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td>MedImmune / AZ.</td>
<td>Innate</td>
<td>$250</td>
<td></td>
<td>Phase II</td>
<td>Cancer</td>
</tr>
<tr>
<td>Allergan</td>
<td>Merck</td>
<td>$250</td>
<td></td>
<td>Phase II</td>
<td>Neurology</td>
</tr>
<tr>
<td>Novartis</td>
<td>Aduro</td>
<td>$200</td>
<td>$25</td>
<td>Preclinical</td>
<td>Cancer</td>
</tr>
<tr>
<td>Celgene</td>
<td>Juno</td>
<td>$150</td>
<td>$850</td>
<td>Phase II</td>
<td>Diversified</td>
</tr>
<tr>
<td>Celgene</td>
<td>Nurix</td>
<td>$150</td>
<td></td>
<td>Discovery</td>
<td>Diversified</td>
</tr>
<tr>
<td><strong>MerckKGaA</strong></td>
<td>Intrexon</td>
<td>$115</td>
<td></td>
<td>Discovery</td>
<td>Cancer</td>
</tr>
<tr>
<td><strong>Celgene</strong></td>
<td>Lycera</td>
<td>$105</td>
<td></td>
<td>Phase I</td>
<td>Cancer</td>
</tr>
<tr>
<td>Janssen</td>
<td>Hanmi</td>
<td>$105</td>
<td></td>
<td>Phase I</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td>Bayer</td>
<td>Ionis (fka ISIS)</td>
<td>$100</td>
<td></td>
<td>Phase II</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td><strong>DiaVax</strong></td>
<td>City of Hope</td>
<td>$100</td>
<td></td>
<td>Phase I</td>
<td>Viral Infection</td>
</tr>
<tr>
<td>Bayer</td>
<td>Ionis (fka ISIS)</td>
<td>$100</td>
<td></td>
<td>Phase II</td>
<td>Hematologic</td>
</tr>
<tr>
<td><strong>Merck</strong></td>
<td>NGM</td>
<td>$914</td>
<td>$106</td>
<td>Preclinical</td>
<td>Endo/Meta</td>
</tr>
<tr>
<td>Vertex</td>
<td>Parion</td>
<td>$80</td>
<td></td>
<td>Phase II</td>
<td>Pulm/Resp</td>
</tr>
</tbody>
</table>

Highlights indicate Phase I Licensing

### Valuation of Companies

<table>
<thead>
<tr>
<th>Company</th>
<th>Valuation (USDm)</th>
<th>Development Stage of lead drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agios Pharmaceuticals, Inc.</td>
<td>$1,829</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Karyopharm Therapeutics, Inc.</td>
<td>$288</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Dicerna Pharmaceuticals, Inc.</td>
<td>$68</td>
<td>Phase 1</td>
</tr>
<tr>
<td>Immune Design Corp.</td>
<td>$167</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Heat Biologics, Inc.</td>
<td>$14</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Loxo Oncology, Inc.</td>
<td>$514</td>
<td>Phase 1</td>
</tr>
<tr>
<td>Epizyme, Inc.</td>
<td>$597</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Kite Pharma, Inc.</td>
<td>$2,609</td>
<td>Phase 1/2</td>
</tr>
<tr>
<td>Idera Pharmaceuticals, Inc.</td>
<td>$185</td>
<td>Phase 1/2</td>
</tr>
<tr>
<td>Ignyta, Inc.</td>
<td>$213</td>
<td>Phase 1/2</td>
</tr>
<tr>
<td>Inovio Pharmaceuticals, Inc.</td>
<td>$716</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Five Prime Therapeutics, Inc.</td>
<td>$1,150</td>
<td>Phase 1</td>
</tr>
<tr>
<td>OncoMed Pharmaceuticals, Inc.</td>
<td>$387</td>
<td>Phase 2</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>$672</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Licensing Deals

<table>
<thead>
<tr>
<th>Licensing Deals</th>
<th>Upfront (includes equity &amp; cash) USDm</th>
<th>Milestone payments (USDm)</th>
<th>Upfront Payment as % of Total</th>
<th>Total deal size</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>999.8</td>
<td>1835</td>
<td>100%</td>
<td>2,012.3</td>
</tr>
<tr>
<td>Mean</td>
<td>87.6</td>
<td>433</td>
<td>22.9%</td>
<td>514.6</td>
</tr>
<tr>
<td>Median</td>
<td>35.0</td>
<td>309</td>
<td>10.3%</td>
<td>363.5</td>
</tr>
<tr>
<td>Low</td>
<td>1.0</td>
<td>0</td>
<td>0.7%</td>
<td>1.0</td>
</tr>
</tbody>
</table>

The average total deal size is $514.6m, and the median deal size is $363.5m.
Sample News Flow in the next 12 Months

- Patent filings on mimotopes (2H, 2016)
- Patients dosed in the Phase 1b/2 trial in gastric cancer (1H, 2017)
- Recruitment progress and interim Phase 1b/2 data (1H, 2017)

- First mimotope drug candidate identified (1H, 2017)
- Preclinical *in vivo/vitro* results (2H, 2017)
- Final Phase 1b/2 trial readout (2H, 2017)
IMU broadens pipeline with acquisition from Baker IDI

- Exclusive agreement with Baker IDI
- Oncology rights to develop a portfolio of small molecule arginine modulators for cancer treatment
- Arginine is a critical amino acid for the health of cancer fighting T-cells and depletion of it limits the effectiveness of T-cells to fight tumors
- Baker IDI compounds increase the availability of arginine in the cellular environment
- Minimal cost and resources required for POC in 2017
- New patent filed to protect compounds in the field of cancer and immuno-oncology, including combination with checkpoint inhibitors
A Team with Track Record in Drug Development

Leslie Chong  
*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  
*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; **Imugene is his only Board seat worldwide**

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

Prof. Ursula Wiedermann  
*Chief Scientific Officer*  
- Co-inventor of Her-Vaxx; inventor of mimotope platform technology  
- Professor of Vaccinology at Medical University of Vienna

Dr. Nick Ede  
*Chief Technology Officer*  
- Over 25 years peptide vaccine and drug development  
- Former CTO Consegena, CEO Adistem Ltd, CEO Mimotopes P/L, COO EQiTX Ltd (ZingoTX & VacTX)  
- VP Chemistry Chiron (now Novartis), Research Fellow CRC Vaccine Technology

Dr. Anthony Good  
*Clinical Program Manager*  
- Over 15 years oncology & immunology experience in global clinical development programs. Integral to the development of significant new medicines including Viagra, Revatio, Lipitor, Selzentry and Somavert.  
- Ex Pfizer Global Research and Development, Covance Clinical and Periapproval Services and Western Sydney University
Business Strategy and Partnering Opportunities

Phase 1b
Gastric Study

Phase 1b
Mimotope + others

License /Partner

Big Pharma?

2017

2017-2018

2017-2018?
Our Stock

ASX:IMU, ISIN: AU000000IMU9

Market Cap (22/Dec/16) $32.5M AUD, $23.5M USD
Ordinary Shares 2.17 billion
12 month price range 0.7 cents – 2.1 cents AUD
Avg daily volume 10.5M shares (last three months)
Investment to Date ~$12.2 m
Cash & Equivalents $3.82M as of 22/Dec/2016

Options on issue (as at Dec. 2016)

<table>
<thead>
<tr>
<th>No of options</th>
<th>Exercise Price</th>
<th>Expiry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Listed (IMUO)</td>
<td>$0.015</td>
<td>31-Mar-17</td>
</tr>
<tr>
<td>Unlisted</td>
<td>$0.0173*</td>
<td>30-Oct-17*</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$0.0155*</td>
<td>18-May-17*</td>
</tr>
</tbody>
</table>

Substantial holders (as at Dec. 2016)

<table>
<thead>
<tr>
<th>No. of Shares</th>
<th>% Capital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum Asset Management</td>
<td>213,846,553</td>
</tr>
<tr>
<td>Webinvest Pty Ltd &lt;OLSB Unit A/C&gt;</td>
<td>101,000,000</td>
</tr>
<tr>
<td>National Nominees Limited</td>
<td>66,424,732</td>
</tr>
<tr>
<td>Tisia Nominees</td>
<td>65,666,666</td>
</tr>
<tr>
<td>Sarah Cameron</td>
<td>51,817,073</td>
</tr>
</tbody>
</table>

* Average
IMU’s Value Proposition

✓ Promising science with impeccable provenance in the hottest area of cancer today – immuno oncology

✓ Broad Pipeline: HER-Vaxx & Mimotopes

✓ Breast Cancer clinical trial complete & on the cusp of recruitment on our second Phase 1b/2 clinical trial in gastric cancer

✓ Tight share register with leading Fund Manager, Platinum Asset Management

✓ Frequent, rich, quality news flow ahead

✓ Axel Hoos Sr. VP of immuno – oncology at GSK, plus team with successful track record in drug development

✓ Low market cap - undervalued against ASX peers
Contact

Leslie Chong
Chief Executive Officer
leslie.chong@imugene.com
+61 458 040 433
Appendix
# Imugene Science Advisory Board

<table>
<thead>
<tr>
<th>Name</th>
<th>Background and Specializations</th>
</tr>
</thead>
</table>
| **Christoph Zieliniski**    | • Director, Clinical Division of Oncology and Chairman, Department of Medicine at Medical University Vienna, Austria.  
                               • Coordinator of the Comprehensive Cancer Center at Medical University Vienna and the General Hospital in Vienna, Austria.  
                               • President, Central European Cooperative Oncology Group (CECOG). |
| **Ursula Wiedermann**       | • Chief Science Officer  
                               • Professor of Vaccinology and Head of the Institute of Specific Prophylaxis and Tropical Medicine of the Medical University Vienna.  
                               • Speaker of the newly founded Centre for Geographic Medicine at the Medical University Vienna |
| **Neil Segal**              | • Oncologist at the Memorial Sloan Kettering Cancer Center.  
                               • He holds a Doctorate of Medicine and Philosophy from University of the Witwatersrand in South Africa. |
| **Yelena Janjigian**        | • Medical oncologist at the Memorial Sloan Kettering Cancer  
                               • Specializes in the treatment of malignancies of the gastrointestinal tract, including esophagus and stomach cancers. |
**Phase Ia 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

---

Patient Characteristics – Ages 55-84 *

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Age</th>
<th>Metas. disease since</th>
<th>Prior chemotherapy</th>
<th>Current antihormonal therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>Oct. 2006</td>
<td>no</td>
<td>Anastrozol</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>May 2004</td>
<td>yes (1 adj)</td>
<td>Fulvestrant</td>
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### Safety and Tolerability – Few Grade 1 Local Reactions, None Systemic*

<table>
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<th>Patient ID</th>
<th>Local vaccination reaction grade</th>
<th>Systemic grade 3/4 toxicity</th>
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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

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

Antibody and cellular responses in human

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<th>Pat. #</th>
<th>Peptide-specific ab</th>
<th>HER2-specific ab</th>
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HER-Vaxx breast cancer vaccine – Phase 1 trial 10 μg group

- 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

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

No toxicity, in Particular No Cardiotoxicity

Rat cardiomyocytes

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

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