IMUGENE

HER2 +ve gastric and breast cancer vaccines

**Imugene (ASX; IMU)** is an oncology focused biopharmaceutical company developing HER2 +ve gastric and breast cancer vaccines

# Investor Update Issue 1



## Welcome to the first issue of the Imugene Ltd Investor Update newsletter for 2014.

A lot has happened in your company at the end of 2013, and the Investor Update is one way we plan to keep investors up to date with our activities and progress.

Firstly, let me thank you for your support of the Company to date. It is your vision and ability to provide the Company with the backing it requires that lets us pursue our goals of providing new treatment options and, following the acquisition of Biolife Science, more specifically for cancer patients.

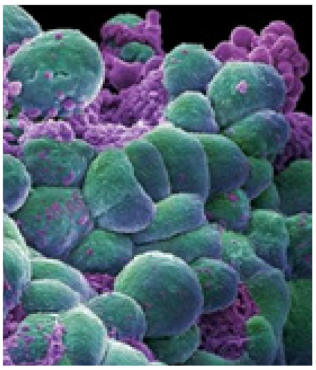
In October last year Imugene announced plans to acquire the business of Biolife Science, whose lead product is HER-Vaxx. Biolife has the rights to a novel therapeutic cancer vaccine platform that has been developed by scientists at the University Medical School in Austria. The scientists have developed a peptide-based vaccine that induces a polyclonal antibody response against HER-2/neu associated tumours, including breast cancer and gastric cancer ("HER-Vaxx"). In December Imugene completed this acquisition.

Message from the Executive Director

Dr Nick Ede

Imugene Ltd
Executive Director

### HER-Vaxx is the Company's core focus in 2014.



In this newsletter we have included an extensive Q&A on many of the questions we have received recently.

During this exciting period we have also strengthened our Board to reflect our ambitions to develop HER-Vaxx. This included the appointment of Dr Axel Hoos as non-executive director in December. Dr Hoos is currently the Global Vice President of Oncology R&D at GSK, one of the largest pharmaceutical companies globally and a strong player in Oncology.

We are particularly excited by the potential for HER-Vaxx to provide a new commercially available treatment option for cancer patients globally, and look forward to providing further information on our progress over the coming months.

## About HER-Vaxx - a therapeutic cancer vaccine for the treatment of gastric and breast cancer


In December last year we successfully acquired from Biolife Science a potential novel therapeutic cancer vaccine, HER-Vaxx, that has to date been shown to trigger an immune response to HER-2 present on certain types of breast cancers. HER-Vaxx is a B-cell peptide cancer vaccine that induces an antibody response targeted against tumours that exhibit a great number of HER-2 receptors upon tumour cells.

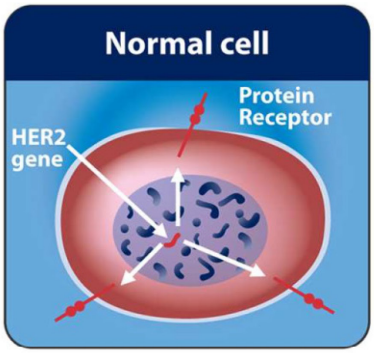
HER-2 communicates molecular signals from outside the cell to inside the cell and controls the activation of genes, which in turn control cell multiplication, proliferation and tumour cell spread. In some cancerous cells, including those present in certain types of breast and gastric cancer, HER-2 is over-expressed, causing cancer cells to reproduce uncontrollably. HER-2 is over-expressed in 15-30% of invasive breast as well as in 7-34% of gastric cancers.

One of the most prevalent and effective treatments for HER-2 positive cancers is a pharmaceutical known as Trastuzumab. Trastuzumab is a monoclonal antibody that was developed by Roche Ltd and Genentech Inc. and is marketed as "Herceptin®". Although Herceptin® has proven to be effective in the treatment of early stage and metastatic breast cancer, a course of Herceptin® treatment can cost as much as US$100,000 per year.

The original studies of Herceptin® indicated that it improved overall survival in late-stage (metastatic) breast cancer from 20.3 to 25.1 months. It is commonly administered in conjunction with chemotherapy.

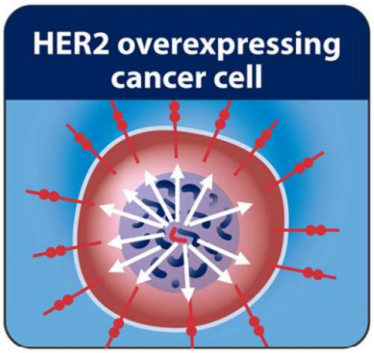
Herceptin® operates by binding to one particular site (epitope) on HER-2 and blocks the growth signals that cause the cancerous cells to proliferate. It acts to slow the rate of growth of cancerous cells and acts through several mechanisms to kill tumour cells.

The following diagram shows how cell growth is controlled in normal and HER-2 overexpressing cells and how Herceptin® slows the rate of growth of cancerous cells:



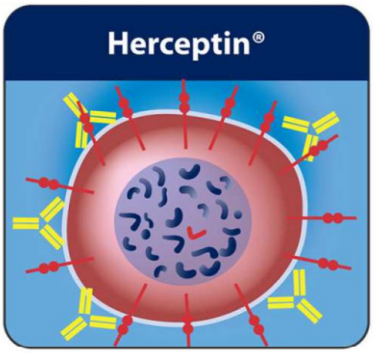

**In normal cells, the HER2 gene produces a protein receptor on the cell surface.**

**These growth-like receptors signal the cell to divide and multiply.**




**Cancer cells that over-produce HER2 gene produce many more receptors.**

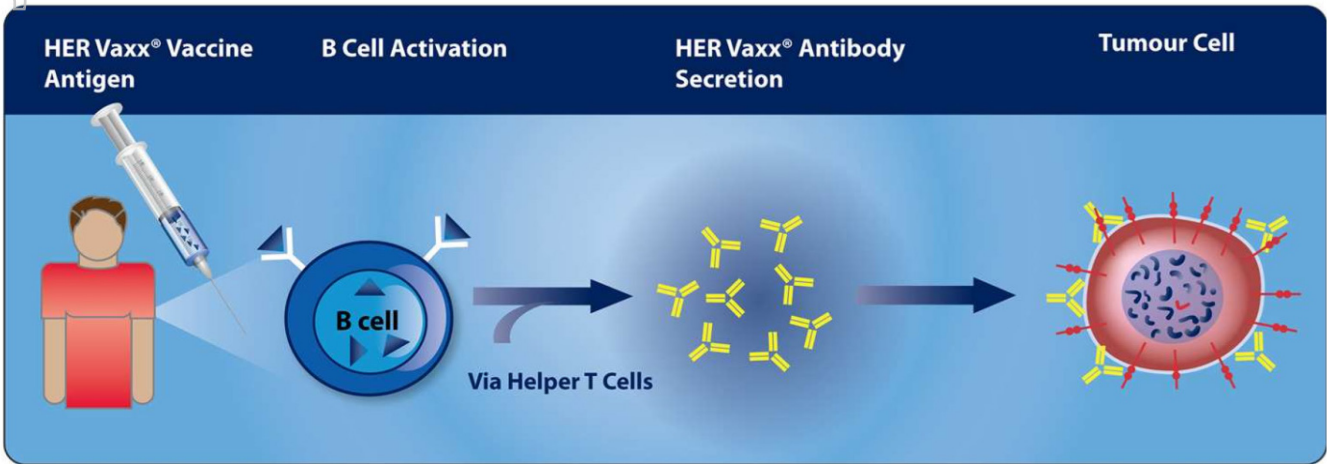
**This triggers the cell to divide and multiply at an accelerated rate, thus contributing to tumour growth.**




**Herceptin® is an injected synthetic HER2 antibody. It binds to the HER2 receptor sites and blocks their growth signals.**

**In this way, the HER2 antibody is thought to slow the rate of growth of cancer cells.**

HER-Vaxx's delivery mechanism is different, and potentially superior, to that of Herceptin®. Instead of regularly injecting a monoclonal antibody that recognises only one specific segment of HER-2, HER-Vaxx comprises several peptides that, when introduced to the body, are designed to induce a polyclonal antibody response that targets more than one site of HER-2. It therefore may potentially elicit a more powerful anti-tumour effect and should result in the treatment being able to target cancer at an earlier stage than Herceptin®. The following diagram illustrates how HER-Vaxx is intended to work:




Rather than injecting a ready-made antibody, HER-Vaxx is a novel therapeutic cancer vaccine that activates a patient's own immune system to produce its own antibodies and also cellular immune mechanisms, effectively turning the patient's body into a "Herceptin® factory". In contrast to Herceptin®, which requires regular injections, with HER-Vaxx the body produces a constant supply of antibodies.

Furthermore, because HER-Vaxx is a therapeutic vaccine, it may achieve a long-lasting immune response and immunological memory, which does inhibit tumour re-occurrence.

## **Meet Dr Axel Hoos -** Imugene's new non-executive director

Dr Axel Hoos is Vice President, Oncology R&D at GlaxoSmithKline where he directs clinical and translational research on the molecular mechanisms of cancer and tumour-host interactions in order to optimize patient outcomes through the rational combination of therapies.

Axel has a wealth of experience in cancer drug development. Prior to his current role, Axel was the medical lead in immunology/oncology at Bristol-Myers Squibb where he developed the Yervoy monoclonal antibody in melanoma and other indications. Yervoy is the first therapy to extend survival in metastatic melanoma.

Before BMS, Axel was Senior Director of Clinical Development at Antigenics Inc., a biotechnology company, which develops therapies for cancer and infectious diseases. Axel studied medicine at Heidelberg University, Heidelberg, Germany and received his Ph.D. in Molecular Oncology for work in molecular biology and tumor immunology at the German Cancer Research Center, Heidelberg. He trained in surgery with a focus on surgical oncology at the Technical University in Munich and further in surgery, molecular pathology and tumor immunology at Memorial Sloan-Kettering Cancer Center in New York.

Axel has previously been Co-Director of the influential think-tank Cancer Immnunotherapy Consortium, which is comprised of the Key Opinion Leaders in the international cancer immunotherapy community and also the author of a seminal paper published October 2011 - "A methodological framework to enhance the clinical success of cancer immunotherapy" - Nature Biotechnology October 2011. You can download for free on our website an important paper published by Axel and colleagues titled "The Immuno-Oncology Framework" – Enabling a New Era for Cancer Therapy.

## HER-Vaxx Q&A

### 1. What is the history of the technology?

The science represents over a decades' work from a group of prominent European oncologists and immunologists/vaccinologists from the Medical University of Vienna, Austria.

### 2. How well known are the key people/scientists involved with HER-Vaxx?

The founders are highly regarded in the European and international oncology communities.

- Professor Zielinski is Director of the Clinical Division of Oncology and Chairman of the Department of Medicine at the Medical University of Vienna, Austria. He serves as coordinator of the Comprehensive Cancer Centre at the Medical University of Vienna (www.ccc.ac.at) and the General Hospital in Vienna, Austria and is President of the Central European Cooperative Oncology Group (CECOG, www.cecog.org).
- Professor Wiedermann is Professor of Vaccinology and Head of the Institute of Specific Prophylaxis and Tropical Medicine of the Medical University Vienna. Currently she also has an appointment as Visiting Professor at the University in Göteborg, Sweden.
- Dr Axel Hoos is V-P Oncology R & D at GlaxoSmithKline

### 3. The therapeutic vaccine has been in a 10 patient, Phase 1 trial. Why do you think the vaccine could work?

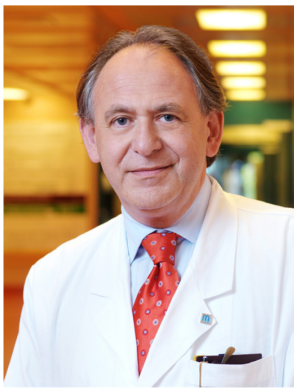
Antibodies generated by B-Cell epitopes such as HER-Vaxx have passed the acid test of clinical trials and the market validation of targets.

Phase 1 trials are typically small to meet their safety endpoints. Notwithstanding this, in addition to demonstrating safety, HER-Vaxx's Phase 1 trial showed:

- Patients developed anti-HER-2 antibodies – HER-2 has shown its importance as a target in the treatment of cancer. Herceptin, which targets HER-2 has been approved in gastric and breast cancer;
- Due to the specific adjuvant used in the vaccine patients also developed significant levels of interferon-gamma as well as levels of TNF-alpha upon in vitro re-stimulation with our vaccine;
- Evidence that vaccination with our vaccine significantly reduced T Regulatory (T Regs) cells which are known to suppress anti-tumor activity. In gastric cancer, T Regs seem to be particularly enhanced. Since chemotherapy has been shown to reduce T Regs, it is reasonable to expect we will see a signal, as chemotherapy is also combined with our vaccine as we plan in our trial, which has shown to also reduce T Regs,

Combined, we believe that these results are robust for a Phase 1 trial, above and beyond demonstrating safety.

What gives additional confidence that the cancer vaccine will work is that, unlike many other vaccines, HER-Vaxx's cancer vaccine target (HER-2) has been previously validated by Herceptin. In other words, thanks to Herceptin, it is well known that creating antibodies against HER-2 may be an effective cancer treatment.



Professor Zielinski

Professor Wiedermann

**Phase I Breast Cancer Trial published in peer reviewed international journal**

### 4. The Phase 1 trial was done in breast cancer patients – why are you doing the Phase 2 in gastric cancer?

Since our molecular target of HER-2, occurs across many cancers (not just breast cancer), we have chosen a cancer type where the recruitment of patients may be easier and where the trial will be shorter – gastric/stomach cancer.

A Phase 2 clinical trial in gastric cancer is likely to take a shorter time to complete, and is therefore is expected to cost less – and from perspective of both patients and investors, getting the results sooner, is better.

The target of our drug is the same whether in breast cancer or gastric cancer.

### 5. Is the intellectual property and patent position well protected?

Yes the IP is robust. We have 3 patent families – one which covers the peptide antigens (epitopes) derived from HER-2/neu, one which covers the therapeutic cancer vaccine that is specifically being manufactured for the trial and is of commercial interest, and three, an exclusive license in oncology (cancer) for the virosome vaccine delivery technology.

### 6. How big is the gastric cancer market in terms of patients and drug sales?

Gastric or stomach cancer, is the second most common cause of cancer-related death in the world, and is the fourth most commonly diagnosed cancer, with over 1,000,000 cases of stomach cancer diagnosed each year.

Gastric cancer drugs are forecast to experience robust growth over the next decade increasing from just $800 million in 2010 to nearly $1.4 billion in 2020. This will be driven by the take-up of Roche's Herceptin and the possible launch of another drug under development.

### 7. How long will it be before you can start the Phase 2 trial?

It will take about 12 months + before the Phase 2 trial will commence – that period will be spent manufacturing the cancer vaccine.

### 8. How long will the trial take to complete?

We have received detailed quotes from international CROs.

Their forecasts indicate that the trial will be recruited in about 12 months.

### 9. What type of trial is it and where will it be run?

This is a gold standard Phase 2 clinical trial of a very robust nature in terms of design: double blind; randomized; and placebo-controlled.

Data emerging from trials of this design are highly regarded.

Very few companies in Australia are conducting Phase 2 trials to this high level. The plan is to do the Phase 2 trial in Eastern Europe.

### Gastric Cancer Facts

- Gastric cancer is a common disease with a high death rate
- 4th most commonly diagnosed cancer
- 2nd most common cancer in men and 3rd most common in women
- Japan, Korea and China have the highest gastric cancer rates in the world
- Treatment of gastric cancer is: surgery; chemotherapy & radiation
- Surgery is the mainstay of curative treatment
- The outlook for advanced gastric cancer is poor with a median survival of only 7-10 months
- Approximately 7-34% of gastric cancer patients are Her-2 positive
- The anti-HER-2 drug, Herceptin, is now approved for gastric cancer & is given in combination with standard chemo
- This combination has helped patients to live about 2.7 months longer than patients who received chemo alone

## Imugene Facts

**Listings**
Australian Securities Exchange (ASX)

**Stock code**
ASX: IMU

**Issued capital Ordinary shares**
940 million

**Market capitalisation based on share price of 0.02 cents**
18 Million

## Board and Management

**Mr Paul Hopper**
Executive Chairman

**Dr Nick Ede**
Executive Director

**Dr Axel Hoos**
Non-executive Director

**Mr Phillip Hains**
Joint company secretary and Financial Controller

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## Forward looking statement

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