

## IMUGENE (ASX; IMU)



Dear Shareholders

Welcome to the fourth Imugene newsletter and the second since my appointment as CEO in August 2014. I joined at a busy period in the development of Imugene's HER-Vaxx and since then the Company has reported good progress on:

- Manufacture of HER-Vaxx -- appointment of Bacchem to manufacture the key peptides for HER-Vaxx
- Appointment of Professor Weiderman's laboratory at University of Vienna to undertake additional preclinical testing necessary for completing an IND with the US Food & Drug Administration (FDA)
- Finalising the best formulation of HER-Vaxx to prepare for GMP-compliant manufacture of sufficient quantity for next year's gastric cancer clinical trial.

We have also been busy meeting Australian investors to raise sufficient funds to begin the gastric cancer trials. On 5 November we announced a placement of \$2.25m with new and existing investors at 1.0 cent per share. This included a substantial investment by Non-Executive Director Otto Butula who has been a great asset to Imugene both in his new position on the board and as an investor.

With the placement we also announced a shareholder purchase plan (SPP) for all our shareholders, enabling small and large shareholders to subscribe for stock on the same terms. We trust our smaller shareholders will take the opportunity to make an investment in this very exciting technology while it is still comparatively unknown to the wider investment community.

We are looking forward to dramatically expanding our reach to gain recognition from the wider investment community both domestically and overseas and I will undertake a number of initiatives to make that happen. Indeed I have already been to the US to begin raising the Company's profile with US investors.

### OUTLOOK

A number of initiatives in the coming months are underpinned by the funds from our placement and SPP. First and foremost is the manufacture and preclinical work required to support an investigational new drug application (IND) for our Phase Ib/II trial with the US FDA.

We are also looking forward to finalising the clinical trial protocol and appointing a well-qualified clinical research company to manage and execute our high quality clinical trial for HER-Vaxx. The result of this will be to start our Phase Ib/II clinical trial in the second half of next year for patients with metastatic HER2 positive gastric cancer.

We will continue to spread the word about our exciting asset to investors and potential pharmaceutical partners. While we have started improving our profile with investors – starting with the fund raising – such efforts are only in their infancy and we look forward to ramping up the outreach.

We are preparing a robust trial which will be designed to impress potential large pharmaceutical company licensees. The robust trial design features include being blinded, randomised and placebo controlled. For a Phase II trial run by a biotechnology company this is unusually robust, but the additional level of statistical rigour will impress our target licensees.

Over the next year we will actively inform potential partners about our technology and the trial so that when Imugene reports results, potential partners will already know us, anticipate the data and be ready to move to a license.

In the remainder of this newsletter we outline why Imugene's technology has great potential.

I often get asked why we think we can improve on the work of pharmaceutical and biotech giants Roche and Genentech in finding a superior means by which to target HER2. The answer is that we simply aim to build upon the work of those two pharmaceutical giants, not substitute it, and the following section aims to explain the basis of this belief.

In the meantime, we at Imugene are enthused by the opportunity offered by HER-Vaxx and look forward to working together to deliver real milestones for you our shareholders.

Yours faithfully  
Charlie Walker

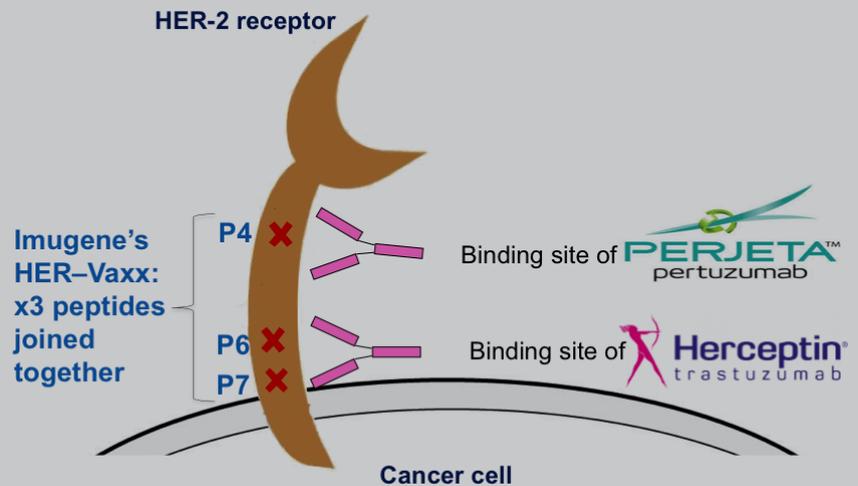


## SHAREHOLDER PURCHASE PLAN (SPP) INFORMATION

Record date	7pm AEDT Friday 31 October
Opening date	Friday 7 November
Closing date	Friday 28 November
Allotment date	Monday 8 December
Holding statement dispatch	Tuesday 9 December
Quotation date	Wednesday 10 December

Issue price	\$0.01 per share (21% discount to 30 day VWAP)
Application amounts	Minimum \$1,000 (100,000 shares) up to maximum of \$15,000 (1,500,000 shares) in staged increments of \$1,000, e.g. \$2,000, \$3,000, \$4,000 etc

# AN UPDATE ON THE PROMISING SCIENCE BEHIND HER-VAXX



HER-Vaxx is foremost a peptide vaccine or immunotherapy which aims to enable a patient's immune system to fight cancer. The peptide component in HER-Vaxx is the payload to which the immune system generates cancer-fighting antibodies. Elizabeth Mittendorf, associate professor of surgical oncology, MD Anderson Cancer Center recently stated, "Peptide vaccines have the benefit of being easy to construct and manufacture on a large scale, they're inexpensive, and very importantly they are off-the-shelf therapy."

To deliver the immunotherapy we have chosen the industry validated "influenza virosome" platform. Importantly this platform is used by others such as J&J-owned Crucell to deliver its influenza and Hepatitis A vaccines, having sold more than 70 million doses in about 40 countries.

B cells are the main players of the humoral (antibody) immune response. They generate antibodies towards pathogen-derived molecules; or in our case, at cancer cells. We learnt in the first newsletter of 2014 that HER-Vaxx is a B-cell peptide epitope cancer immunotherapy that triggers an immune response to cancer-associated receptor HER2/neu. We also learnt that the monoclonal antibody drug Herceptin® operates by binding one particular site (epitope) on the HER2/neu receptor and this blocks the growth signals that trigger new cancer cell growth.

In 2012 Roche launched a second-generation HER2-binding monoclonal antibody drug named Perjeta™. Perjeta™ is a more potent version of Herceptin® and inhibits HER2's function by targeting a region of the HER2 receptor responsible for a process known as receptor dimerization. However unlike Herceptin® and Perjeta™, HER-Vaxx generates antibodies to three separate regions of HER2/neu by activating the patient's own adaptive humoral immune response. These three regions (depicted in the figure above) are located close to the binding regions of Herceptin® and Perjeta™. How is this important for Imugene's HER-Vaxx?

In September Roche announced final data from its Phase III CLEOPATRA study that showed people with previously untreated HER2-positive metastatic breast cancer who received Perjeta™, Herceptin® and chemotherapy lived a median of 56.5 months compared with 40.8 months for people who received Herceptin® and chemotherapy alone. Adding Perjeta™ to treatment with Herceptin® and chemotherapy resulted **in the longest survival observed to date in a clinical study of people with HER2-positive metastatic breast cancer.**

Imugene's scientists in Europe have already demonstrated in preclinical animal models that by combining the three B-cell peptides into a single fusion peptide antigen, HER-Vaxx elicits a specific protective immune response. This was as tested in our Phase I breast cancer trial. It was superior to that elicited by the respective separate single-epitope peptides. That is, linking the three individual B cell peptides of HER2/neu into a single peptide antigen results in an advantageous synergism analogous to the Roche Phase III trial combining Perjeta™ and Herceptin®.

This is very encouraging for Imugene and it's this sort of potential that drives us all at Imugene to drive HER-Vaxx into the clinic as rapidly as we can.

#### **Dr Nicholas Ede**

Head Of Manufacturing and Operations

## IMUGENE CEO CHARLES WALKER DISCUSSES THE HER-VAXX OPPORTUNITY

**Q: YOUR COMPANY HAS A LEAD TECHNOLOGY KNOWN AS HER-VAXX. WHAT IS HER-VAXX?**

A: "HER-Vaxx is loosely described as a drug and it aims to fire up a patient's immune system to enable a patient to fight their own cancer. The trouble with cancer is it can't be seen on whole by one's immune system, so we aim to fix that."

**Q: MY UNDERSTANDING IS THAT IT WORKS IN THE SAME WAY AS THE EXISTING DRUG HERCEPTIN. WHY THE NEED FOR A NEW THERAPY?**

A: "Good point. We believe our approach has got potential to produce benefits over Herceptin in a number of different ways. Ideally, we would like it (HER-Vaxx) to be more efficacious, but even if it is not more efficacious, it could well add other benefits, such as (improved) safety or toxicity over Herceptin. There are a number of ways it can improve on Herceptin."

**Q: SO YOU HAVE A DRUG THAT WORKS LIKE HERCEPTIN, BUT COULD WORK BETTER THAN HERCEPTIN. HERCEPTIN COMMANDS A \$6-7 BILLION DOLLAR GLOBAL MARKET PER ANNUM. CAN YOU PUT THAT INTO PERSPECTIVE FOR INVESTORS?**

A: "Herceptin is a very successful drug that has been created by some of the leading scientists in the industry. We are not saying we are doing something that they can't. We are taking it to the next level. So, while Herceptin attacks one particular place on (receptor) HER2, we attack three places.

"We do know that attacking HER2 gets the result and improves the clinical outcomes, so if we can attack it in a better way -- and we have been researching this for years -- we have got every reason to believe that we can improve on the outcomes of Herceptin.

"If we improve on the mechanism of Herceptin, we know we have got a serious, valuable asset here."

**Q: YOU ARE DOING TRIALS IN BREAST AND GASTRIC CANCERS - WHAT IS THE LEAD INDICATION?**

A: "Our Phase 1 was done in breast cancer and that was done in ten patients in Vienna, one study and broadly speaking, we showed we could set up an immune response and we could produce antibodies.

"In the Phase 2, we will do it in a new indication called gastric cancer.

"It is a better indication for us to pursue. It will take less money to pursue it. It is more of a lethal cancer, if you like. Survival is less than it would be for breast cancer. So we have got a better chance of showing an effect in a shorter period of time with that trial."

**Q: WHAT ARE THE NEXT KEY INFLECTION POINTS?**

A: "We have got to initiate our next trial. The next trial will be a Phase 1b trial to start mid-2015. It will lead straight into a Phase 2 trial.

"The Phase 1 part of the next trial will be open-label, so we will be able to get a good steer from that really quickly. It will examine dose and all sorts of toxicity and other effects. It will roll straight into the Phase 2.

"So next year we will be starting the trial and we will be finishing the manufacturing. We may be in a position to report early observations from the trial.



*This is an edited transcript of a video interview with Imugene CEO Charles Walker. For further information please go to [www.imugene.com](http://www.imugene.com)*

**Q: WHAT IS THE COMPANY'S CASH POSITION AT THE MOMENT AND DO YOU HAVE ENOUGH FUNDING TO PROGRESS NEXT STAGE TRIALS?**

A: "At the end of June we had \$1.8 million in cash on the balance sheet. We have initiated a manufacturing program that will cost us a million dollars this year and that will manufacture sufficient drug to start our trials.

"The (Phase 2) trial, we would expect to cost between \$3.5 and \$5 million from the beginning right to the end, to the pivotal inflection point. So, we plan to use the capital we have raised to at least conduct our Phase 1b and depending on circumstances at the time, get into the Phase 2 trial."

**Q: CAN YOU OUTLINE YOUR CORPORATE STRATEGY? RECENT ANALYST COVERAGE SUGGESTED YOU WOULD SEEK A MAJOR LICENSING OR PARTNERSHIP DEAL AROUND 2017. IS THAT FEASIBLE AND WHY IS THAT TIME FRAME LAID OUT AT THE MOMENT?**

A: "We have designed this trial to appeal to big pharmaceutical companies. It is statistically rigorous; we have learnt lessons from other immunotherapy trials and the world has been working out how to do these sorts of trials.

"We have been really designing it so when we get our big results, it will be appealing to big pharmaceutical companies. It will answer the questions that they naturally have. Doing a placebo-controlled random trial is more likely to answer their questions than an open-label trial."

**Q: SO YOU WOULD EXPECT TO PARTNER OR LICENSE THIS TECHNOLOGY PRIOR TO PHASE 3?**

A: "Yes, we would. We will let big pharma know now what we are doing. We would not expect to do a deal right now. Our strategy is to get these results and then have the conversation about how to progress the drug with them and hopefully we will have the data in hand with the questions answered that they need."

**Q: SUM UP THE OPPORTUNITY FOR ME: WHY SHOULD INVESTORS BE LOOKING NOW TO IMUGENE?**

A: "This is a critical period because we have spent the last 6-12 months building a high quality company with a high quality set of assets. Going forward it is all coming together. We have got the management and the team in place. We have got the scientific capability. We have got a high quality asset and we have got a valuation discrepancy that no-one else has got.

"Broadly speaking [we feel] there is a value discrepancy that is not reflected in the asset. The asset is very high quality, so I expect to close that gap. Now is the time to invest because the gap is going to close."

## WANT TO KNOW MORE?



For more information on Imugene and how HER-Vaxx works please watch the corporate video. It is available via the Imugene website home page [www.imugene.com](http://www.imugene.com) or at <https://www.youtube.com/watch?v=JZkOhCBDwss>

## IMUGENE AGM

We encourage the attendance of shareholders to the company AGM on Tuesday 25 November.

10:30am Tuesday 25 November  
Marble Room 1  
Radisson Blu Hotel  
27 O'Connell St  
Sydney

For more information please contact:  
Charles Walker  
TEL: +61 450 446 990  
EMAIL: [cwalker@imugene.com](mailto:cwalker@imugene.com)

### IMUGENE FACTS

#### Listings

Australian Securities Exchange (ASX)

#### Stock code

ASX: IMU

#### Issued capital Ordinary shares

1.15 billion

#### Market capitalisation (18 November 2014)

\$12 Million

#### Share Price

1.1 cent

### BOARD AND MANAGEMENT

#### Paul Hopper

Executive Chairman

#### Mr Charles Walker

Chief Executive Officer

#### Mr Otto Buttula

Non-executive Director

#### Dr Axel Hoos

Non-executive Director

#### Dr Nicholas Ede

Head of Manufacturing and Operations

#### Mr Phillip Hains

Joint company secretary  
& Financial Controller

### FOR FURTHER INFORMATION

Mr Charles Walker (Australia)  
CEO

Imugene Limited  
TEL: +61 450 446 990  
EMAIL: [cwalker@imugene.com](mailto:cwalker@imugene.com)  
Suite 1, 1233 High Street Armadale,  
VIC 3143 Australia  
[www.imugene.com](http://www.imugene.com)

Mr Paul Hopper (USA)  
Executive Chairman  
Imugene Limited  
TEL: +1 858 334 5820  
EMAIL: [receptogen@earthlink.net](mailto:receptogen@earthlink.net)  
[www.imugene.com](http://www.imugene.com)

## FORWARD LOOKING STATEMENT

Any forward looking statements in this newsletter 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 newsletter include known and unknown risks. As actual results may differ materially to any assumptions made in this newsletter, you are urged to view any forward looking statements contained in this newsletter with caution. This newsletter 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.