IMUGENE
Developing Cancer Immunotherapies

ASX: IMU

Newsletter December 2020

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CEO UPDATE

Hello and welcome to our latest update on where your company is and what it is doing. You may recall in our last bulletin we said that cancer does not take a holiday.

Sad to say that's still a reality as we slowly come to grips with the social, economic and health implications of COVID-19.

I personally extend the hope that it has not reached into your lives but if it has, may I offer heartfelt sympathy and like our ongoing efforts to defeat cancer, you will also have the strength to fight against its ravages.

In regard to your investment with us, I can extend to you a positive determination that your company is hard at work and progressing well above expectation. In fact I'm happy to report that in the spirit of the season, Christmas has come early. Our Independent Data Monitoring Committee (IDMC) has given our Phase 2 trial with HER-Vaxx a hearty thumbs up and I'll expand upon this milestone later in the bulletin.

We have also received guidance from the U.S. FDA on both of our CF33 clinical development pathways for CHECKvacc and VAXINIA, our oncolytic virotherapies, for the treatment of metastatic solid cancerous tumours.

Albeit by remote again, we presented two clinical development plans at the prestigious, annual American Association of Cancer Research conference highlighting our work with VAXINIA and PD1-Vaxx.

Our PD1-Vaxx has also recently received several ethics approvals for our Phase 1 clinical trial in the USA and Australia, and a U.S. Food and Drug Administration (FDA) Investigational New Drug (IND) approval.

In another exciting milestone ticked off just this week, the first patient was successfully dosed with PD1-Vaxx in Melbourne, Australia!

We are conducting the PD1-Vaxx Phase 1 trial at three eminent cancer research centres in Sydney and Melbourne and as at the writing of this note to you, all of our Australian sites are actively screening for patients. In our sights is a treatment to tackle Non-Small Cell lung cancer and fitting that November was lung cancer awareness month.

A bit of history – now over five years ago, our field of cancer research was looked upon as a novel but last resort therapy in the treatment of cancer. Immunotherapy is now the frontline.

It's worth mentioning that the regulators have seen the need for early patient access to ground breaking cancer therapies and in some cases, have supported reducing timelines from clinical trials to market provided that the data is solid.

A good example of which was the development process for PD-1 inhibitors Keytruda® and Opdivo®.

Besides our stand alone pursuits we are also focusing on the potential of combination therapies with drugs such as Keytruda® and Opdivo® and other checkpoint inhibitors, who have side effects that include attacks on healthy as well as cancerous cells. Add our Imugene war chest and in combination we steer the immune system away from healthy cells and directly attack the cancerous ones.

Equally as important as the science is the business protection of our efforts and in this regard we're pleased to tell you that we have received a notice of grant from the United States Patent and Trademark Office which further protects our cancer growth-factor B-cell immunotherapy platform through until 2035.

The main focus of this note to you is to tell you all about anti PD-1 therapies and the latest news that our work with HER-Vaxx is on target and then some.

We'll also give you a financial update and I'm happy to tell you we are indeed healthy in that regard.

Due to the isolation effect we all deal with, I have been active in using digital and social media to bring our message across to our many stakeholders.

Our close working relationship with The City of Hope and Ohio State University hospitals and its remarkable group of oncologists and scientists continues to flourish and our joint efforts are proceeding apace.

ANALYST REPORT

We received an analysts report from Roth Capital Partners, the New York based advisory company. It is up on our website in full detail along with an updated report following the release of the HER-Vaxx interim Phase 2 data. The author Jonathan Aschoff, PhD, said in part, "we believe that Imugene has prudently selected areas of unmet need and therefore, ultimately market demand with a high likelihood of clinical success."

> "We are initiating coverage of Imugene with a Buy rating and a 12 month price target of $AUD 0.13," said Dr. Aschoff. However this has already been updated to $AUD 0.20.

I also take great pleasure in introducing you to our newly appointed Chief Medical Officer Dr. Rita Laeufle, M.D. and PhD who will be overseeing our development activities from her base in San Diego. Read about her remarkable career on page 6.

With Warmest Regards,

LESLIE CHONG
IMUGENE CEO

NEWS JUST IN!

OUR FIRST PATIENT WAS DOSED WITH PD1-VAXX IN MELBOURNE

TRIALS UNDERWAY DOWN UNDER & IN THE USA!

Since we last wrote to you, your company has moved from pre-clinical trials to the first stage of human trials.

We have received ethics approval from the external independent Human Research Ethics Committee (HREC) in Australia and Independent Review Boards (IRBs) in the USA, in addition to the coveted US FDA Investigational New Drug (IND) approval to begin Phase 1 clinical trials of our immunotherapy drug, PD1-Vaxx.

What does it mean?

Only 1 in 10,000 promising research breakthroughs will make it into clinical trials due to many factors including successfully obtaining ethical and regulatory approval (eg. FDA IND approval) to proceed.

Ethics approval means that an independent committee of physicians, scientists, and knowledgeable members of the community have carefully reviewed the proposed study, as well as all the necessary pre-clinical safety and efficacy testing of PD1-Vaxx to begin human clinical trials, and consider it scientifically and ethically appropriate to initiate our PD1-Vaxx clinical trial.

FDA IND approval to proceed follows a gold-standard scientific and regulatory review.

At the FDA, dedicated scientists and medical professionals strictly review the entire data set from all the various safety, toxicology, chemistry and manufacturing data.

They only give an approval to trial an experimental drug for cancer patients when convinced it is safe and scientifically appropriate to do so.

Not all anti-cancer investigational products take this route as it is risky. If the FDA declines, or there are on-going queries not met to their satisfaction, it is a mandated clinical hold, which means that a clinical study must not proceed until all FDA queries are satisfactorily answered.

The FDA IND approval for PD1-Vaxx is a huge achievement for cancer patients, our company, and the development of PD1-Vaxx, and one we do not take lightly.

The concept of teaching and inducing the body to generate its own antibodies targeting PD-1 expressing cells represents a significant shift in oncology.

The concept of teaching and inducing the body to generate its own antibodies targeting PD-1 expressing cells represents a significant shift in oncology. Our PD1-Vaxx immunotherapy approach is designed to target lung cancer tumours by interfering with PD-1/PD-L1 binding and interaction and create an anti-cancer attack similar to what Keytruda® and Opdivo® offer in this transformational treatment of a range of cancers.

The Australian Lung Cancer Foundation reports 12,800 Australians are diagnosed with lung cancer every year.

The FDA IND approval for PD1-Vaxx is a huge achievement for cancer patients, our company, and the development of PD1-Vaxx, and one we do not take lightly.

With our ethics approval and an FDA IND a given, where do we go? We dose patients! Our first patient was dosed with PD1-Vaxx this week in Melbourne.

Since last July, we have received three separate approvals to conduct trials at Australian cancer research centres. Chris O'Brien Lifehouse & Macquarie University Hospital in Sydney and Cabrini Hospital in Melbourne are all open to screening.

Not resting on our laurels here in Australia, we are also pleased to tell you that we have received ethics approval at Hackensack University Medical Centre in New Jersey, USA.

We are also planning to initiate the trial at the Mayo Clinic in Phoenix Arizona and The Ohio State University Medical Centre in Columbus, Ohio.

We hope you agree these are significant milestones.

THE BIRTH OF PD1-VAXX

Where did PD1-Vaxx come from? We have been there since its birth and are nurturing it through to maturity but it's rewarding to get a report card from the creator of our latest immunotherapeutic vaccine.

The discovery of PD1-Vaxx by Professor Pravin Kaumaya of Ohio State University, has been published in the prestigious medical journal, Oncoimmunology.

In summation the professor concluded, "we believe the field is poised for many more breakthroughs and significant new improvements in the treatment of patients with cancer for maximum clinical benefits."

Let's briefly go back to the beginning. What motivated the good professor?

An unmet need

Although PD-1 inhibitors Keytruda® and Opdivo® have shown remarkable clinical success in some patients, some 60-70% of patients receiving anti-PD-1 monotherapy treatments such as Keytruda® and Opdivo®, remain resistant to these therapies and they do not respond, hence the unmet need that motivated Professor Kaumaya.

He is a founding father of the new cancer treatment paradigm that is a selective, mechanism-based, targeted therapy using peptide based B-Cell epitopes and peptide immuno-therapeutics that block the growth and spread of cancers by inhibiting oncogenic signalling pathways. They also tend to have far fewer side effects.

"We are excited to begin testing of this vaccine in the United States and Australia to offer new hope to patients with lung and other cancers. Reaching this point where we can transition our findings from the lab to the clinic speaks to the perseverance and dedication of Imugene's clinical and research team — including our research lab staff at Ohio State — to build on the clinical and commercial potential," said Professor Kaumaya.

The report card? An A plus.

About Professor Pravin Kaumaya

- **Professor of The Medicine Department of Obstetric Gynecology at Ohio State University's Wexner Medical Center and The James Comprehensive Cancer Center**
- **Expert in vaccine research with an emphasis on peptide vaccines for cancer**
- **Research focus in tumor immunology, mechanisms of tumor cell, immune cell interactions, and immune mechanisms**
- **Over 130 peer-reviewed articles in major scientific journals**
- **Fellow of the American Association for the Advancement of Science (AAAS), treasurer of American Peptide Society**
- **Conducted first NCI-funded and FDA-approved Phase 1 trial in Stage 4 cancer patients with solid tumors in several indications at The Ohio State University Comprehensive Cancer Center**

TEAM IMUGENE ADDS A STAR TO ITS FIRMAMENT

Your company has a new Chief Medical Officer, Dr. Rita Laeufle, M.D. & PhD.

She is an internationally acclaimed scientist and oncological surgeon, based in San Diego, and she will pick up the reins from Dr. Mark Marino.

We would like to warmly thank Dr. Marino for his time with Imugene.

Dr. Laeufle will also be a member of our executive management team, and she will lead the company's global clinical development, regulatory and medical monitoring activities.

She specialises in immuno-oncology research and has actively coordinated human trials ranging from Phase 1 through to Phase 3. Her accomplishments are many and we are fortunate to have attracted a scientist and surgeon of her calibre.

Her experience quotient is broad and diversified having worked in top tier pharmaceutical companies including Hoffman-La Roche AG and Novartis where she acted in senior level clinical development and leadership roles.

She most recently was Chief Medical Officer at San Diego based Oncolytics Biotech, a company in the foreground of research in oncolytic virotherapy.

She was kind enough to give us a comment on joining Team Imugene, "with a pipeline of innovative immunotherapy vaccines and oncolytic viruses I am enthused to join the wonderful team of experts at Imugene."

We match your enthusiasm Doctor.

"With a pipeline of innovative immunotherapy vaccines and oncolytic viruses I am enthused to join the wonderful team of experts at Imugene."

CHIEF MEDICAL OFFICER, DR. RITA LAEUFLE, M.D. & PHD

THE PD-1 SPACE: A BOOMING MARKET FOR CHECKPOINT INHIBITORS

There is a tremendous amount of activity surrounding the checkpoint inhibitor class of cancer therapies.

Since the 2014 FDA approval of the first PD-1 checkpoint inhibitor drug, Keytruda®, the number of these drugs being developed has skyrocketed. The Cancer Research Institute estimates that there are currently over 1500 clinical trials testing checkpoint inhibitor.

There's a good reason for this surge in the industry. Checkpoint inhibitors have yielded impressive results in a certain percentage of patients with cancer, including those who were not responding to conventional treatments.

As a result of its success, the global immune checkpoint inhibitors market is anticipated to cross US$25 billion by 2022, according to a 2018 report by market research firm RNCOS.

It's also forecasted that checkpoint inhibitors will account for a substantial percentage of all cancer immunotherapy revenue within the decade.

How and why they work

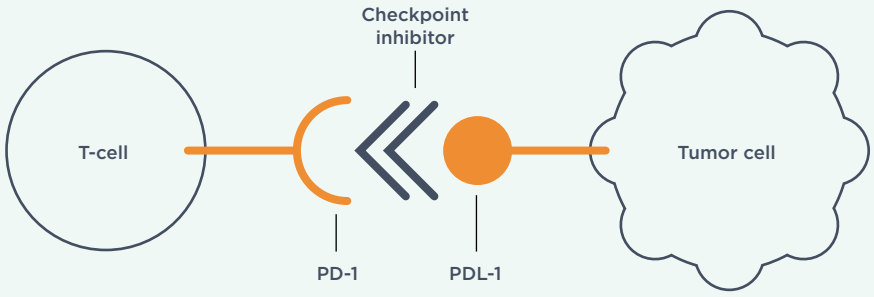
Checkpoint proteins, such as PD-1, exist on the surface of T cells (the bodies assassin cells) and send signals to the immune system letting it know that a cell needs to be removed due to either infection or mutation.

However, cancer cells are able to trick the immune system into treating them as though they are normal cells by over-expressing the ligand to PD-1 called PD-L1 which effectively "turns off" an immune response to that cancer cell by the T cell, which is then able to proliferate. Checkpoint inhibitor drugs work by blocking these proteins from sending these errant "break" signals, allowing the immune system to accelerate and respond appropriately to cancer cells.

"With the rapid rise of industry attention to the PD-1 checkpoint inhibitor, a PD-1 vaccine utilising B-cell technology represents a paradigm shift in cancer immunotherapy."

LESLIE CHONG, IMUGENE CEO

Checkpoint inhibiting drugs block PD-1 and PDL-1 checkpoints from de-activating T-cells



Estimated PD-1/PDL-1 Market Size and Evaluation

Drug	Name	Company	Status	Sales Estimate 2024 (USD $B)
Pembrolizumab	Keytruda®	Merck	Approved	**$22.32**
Nivolumab	Opdivo®	Bristol Myers	Approved	**$10.52**
Atezolizumab	Tecentriq®	Roche	Approved	**$5.29**
Avelumab	Bavencio®	Pfizer	Approved	**$1.7**
Durvalumab	Imfinzi®	AstraZeneca	Approved	**$4.22**
Total For Market*				**$47.33B**

Source: EvaluatePharma, January 2020, Evaluate Ltd
*Not all products list above

HAZARD REFLECTION!

In our fight to address the many forms of cancer, we of course labour aggressively to one day hopefully find a cure, but in that battle there are stages that are equally as important to the patient and their extended family and friends.

The most important is prolonging survival. It's reflected in a statistical formula called Hazard Ratio (HR).

The lower it is, the greater the chance the patient has to experience longer survival.

Our recent HER-Vaxx Phase 2 trial has been evaluated by our Independent Data Monitoring Committee (IDMC) and they've come back to us with a 0.418 HR.

Translated into human terms, that's a median overall survival of 14.2 months for patients receiving HER-Vaxx in combination with chemotherapy as opposed to 8.8 months for patients receiving chemotherapy on its own.

This is a very real, very human consideration and we are both proud and humbled to have achieved such a result.

The background

Our Phase 2 study was designed to measure the efficacy, safety and immune response in 68 patients with late stage, metastatic or advanced gastric cancer. The interim results surpassed our wildest hopes.

The trial had two treatment arms: one group received HER-Vaxx in combination with standard of care chemotherapy, and the other group received standard of care chemotherapy treatment on its own.

Where were these trials conducted?

At multiple cancer research centres in Eastern Europe and India. Patients in these regions have difficulty accessing the currently available antibody treatments Herceptin® and Perjeta® and the level of gastric cancer in these countries is high, due to diet and nutritional issues.

A small win?

No. A significant result! The patients in our trial were all in late stage development of their cancer and HER-Vaxx has given these individuals hope and extra time to be with family.

In a newsletter format like this, we normally just give you a precis of events unfolding, but because our results speak to specific survival benefit, we feel it's appropriate to give you an understanding of the statistics that brought us to this outcome.

How do we determine the overall survival Hazard Ratio (HR)?

It is calculated on the rate of death (ie. survival) when evaluating HER-Vaxx in combination with chemotherapy as compared to chemotherapy alone. We convert this to a ratio so that both groups are represented in the same statistic – the hazard ratio (HR).

If the HR is 1 then the rate of death for both groups is the same. Our HR of 0.418 demonstrates that in the HER-Vaxx plus chemotherapy arm there is 58.2% fewer deaths than on the arm that treated patients with chemotherapy alone.

We also exceeded expectation when compared with the currently available drug Herceptin®. When Herceptin® was combined with chemotherapy, patients had a higher hazard ratio of 0.74, translating to 26% fewer deaths than patients treated with chemotherapy alone.

We accordingly are delighted that our results exceed the overall survival hazard ratio of Herceptin®.

Now, to assist you in the interpretation of our outcomes.

To understand if the results are statistically significant, we look at the p-value compared to a pre-specified alpha.

The pre-specified alpha, is the probability that the effect seen is purely by chance or in other words, the probability that there is a 'false positive' result. If the p value is less than alpha then the result is considered statistically significant, whereas if the p value is greater than alpha then the result is considered not statistically significant.

In our studies we specified that this probability factor would be 10% (pre-specified alpha = 0.1) and the resulting p-value was 0.083! Therefore, we can be rest assured that our hazard ratio was not by chance or a 'false positive' result.

It should also be noted, that we used a one-sided alpha. This was for two reasons:

a) Designing the study with a 1-sided alpha states upfront that we expect there to be a positive treatment effect and setting the value at alpha=0.1 indicates we consider a strong signal for further development if there is less than a 10% risk that the effect we see is purely by chance.

b) The study was designed to detect a strong signal for further development as opposed to filing a registrational study which requires a 2-sided alpha of 5% (alpha = 0.05). Setting alpha at 0.1 is typical in Phase 2 or signal seeking/proof of concept studies, which are generally the precursor to trigger Phase 3 registrational studies to subsequently bring the drug to market.

An alpha of 0.1 is also acceptable to regulatory agencies worldwide for Phase 2 trials especially if they are immunotherapy studies. Why? Because it takes a smaller number of patients/events to complete the study, a cost and resource saving you will appreciate as a shareholder, and it also provides meaningful and significant statistics that could well lead to further development and/or a Phase 3 trials and registration/ marketing of HER-Vaxx.

There is another parameter we use to understand our results and that is, confidence interval (CI). It represents how confident we are that the hazard ratio statistic is accurate.

In our case with a CI of 0.186 to 0.942 we can be 80% confident that our HR will, more often than not, fall close to 0.418 and over 80% confident that the HR will always be less than 1, given that our upper CI is less than 1.

This confirms the most basic message in this explanation and that is HER-Vaxx plus chemotherapy will always prolong life longer than chemotherapy on its own.

As we mentioned at the beginning, a result that cannot be measured in pure statistics... prolonging life. We are equally proud and motivated that HER-Vaxx is providing results well above our expectations.

HER-Vaxx Phase 2: interim analysis:
Efficacy outcome overview

Endpoint	Overall survival intent to treat (Primary)	
Treatment	**Chemo**	**Chemo + HER-Vaxx**
All Patients n=27 (at data cut off)	13	14
Events*	8	4
Hazard Ratio (HR)	0.418	
2-sided 80%CI	(0.186,0.942)	
Log-rank Test (1-sided p-value)**	.083+	

* Death
** Pre-specified alpha at 0.10
+ Statistically significant

A GOLDEN OPPORTUNITY

Monoclonal antibody therapies are a cornerstone of cancer therapies, with a market value totalling over US$65 billion.

The checkpoint inhibitor class of monoclonal antibody drugs have shown strong promise in the treatment of cancer since they first arrived on the scene in 2014.

Demand for these drugs continues to exponentially grow, prompting leading pharmaceutical companies such as Merck, BMS and Genentech/Roche to invest big bucks into their development.

In particular, several I/O drugs, such as Keytruda® and Opdivo® (with sales in 2019 of US$3.8B and $4.9B, respectively), have focused on the PD-1 checkpoint target.

FINANCE

Financial Snapshot
(as at December 2020)

ASX code	IMU
Market cap	$459.77M Dec 2020
52 week high/low	14.0c/1.6c
Cash balance	$26.6M 30 Sep 2020
Industry	Biotechnology

Note: All figures are in Australian dollars. Market capitalisation calculations based on ordinary shares (4.43b) only and excludes the dilutive impact of options outstanding (1.24b).

Top 5 shareholders

Richard Mann and Assoc.	5.66%
Paul Hopper	3.86%
Private Portfolio Managers (PPM)	2.77%
Dr Nicholas Smith	2.57%
HSBC Custody Nominees (Australia)	1.82%

Board & Management

Directors

Ms Leslie Chong
Chief Executive Officer & Managing Director

Mr Paul Hopper
Executive Chairman

Mr Charles Walker
Non-Executive Director

Dr Axel Hoos
Non-Executive Director

Dr Lesley Russell
Non-Executive Director

Dr Jens Eckstein
Non-Executive Director

Senior Management

Dr Nick Ede
Chief Technology Officer

Dr Rita Laeufle
Chief Medical Officer

Dr. Anthony Good
Vice President of Clinical Research

Ms Bonnie Nixon
Project Manager

Mr. Phillip Hains
Company Secretary

Mr Justyn Stedwell
Company Secretary

Scientific Advisory Board

Dr Josep Tabernero
President ESMO, Vall d'Hebron University Hospital Spain

Prof Pravin Kaumaya
OSU, USA

Prof Ursula Wiedermann
Medical University of Vienna

Dr Tanios Bakaii-Saab
Mayo Clinic USA

Dr Neil Segal
MSKCC USA

Dr Yelena Janjigian
MSKCC, USA

Prof Peter Schmid
Barts Cancer Institute at Queen Mary University London

Dr Michael Caligiuri
City of Hope, USA

OV Scientific Advisory Board

Dr Yuman Fong
City of Hope, USA

Prof Prasad Adusumilli
MSKCC, USA

Dr Rebecca Auer
Ottawa Hospital, Canada

FROM THE CHAIR

Hello again! The last time I gave you an update on your company I was sitting in a different chair. This time around I'm working at the same level as I was when in the office chair but when I need a quick break I can step outside and prune a rose before returning to my desk. It's not an ideal world out there but our resolve and energy does not diminish.

Our recent annual report gave you chapter and verse on your company's progress, and I'm proud to say it reflected well on the direction our CEO, Leslie Chong, has taken us.

We have funds in the bank sufficient to cover our current and future activities, and with the recent approvals from independent Ethics Committees and a U.S. FDA IND to proceed with Phase 1 human trials for PD1-Vaxx, and our recent Independent Data Monitoring Committee (IDMC) confirming the results from our Phase 2 trial with HER-Vaxx, I believe you are about to see the faith you've placed in us be acknowledged in a positive fashion.

Broker, Bell Potter and institutional investors agree with me as they have underwritten our recent issue of options and will pick up any that are not converted by the closing date. Their vote of confidence is an important reflection upon our activities and ensures that the full $5.7 million defined in the issue will be realised.

Signing off, I hope you enjoy the highlights we've chosen for your consideration in this brief note. Team Imugene is healthy, energised and as always, looking to create reward for your investment in us.

Your company is in good hands with Leslie and her team bringing results to the table and this year there is a goose in the window and Scrooge is nowhere to be seen.

May I extend a Merry Christmas to you all.

PAUL HOPPER
CHAIRMAN

I believe you are about to see the faith you've placed in us be acknowledged in positive fashion.

IMUGENE
Developing Cancer Immunotherapies

About

Imugene is a clinical stage immuno-oncology company developing a range of new treatments that seek to activate the immune system of cancer patients to identify and eradicate tumours.

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