HARNESSING B-CELLS FOR CANCER IMMUNOTHERAPY
A Paradigm Shift in Play

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Wholesale Investors
September 7 /2018
Notice: Forward looking statements

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Imugene develops vaccines to boost and direct the body’s immune system to specifically target and attack cancer cells.
A BETTER WAY TO MAKE ANTIBODIES TO TREAT CANCER?

In a facility:
For example, Merck’s PD-1 inhibitor Keytruda

Using B-cells in your body
Teaching B-cells to make antibodies using peptide antigens

B-cells are cells in the human body that naturally produce millions of antibodies
Why go for active immunization against cancer?

Difference between passive immuno-therapy and active vaccination
Importance of differentiation in an increasingly crowded market
STRATEGIC ACQUISITION

Ohio State University and Mayo Clinic B-cell peptide vaccine portfolio

- Opportunity to create the pre-eminent, dominant position globally in B-cell peptide vaccines and therapeutics. A catalyst for value creation.

- Professor Kaumaya’s work in the area of check-point inhibitors and tumor-associated antigens such as Her-2, is highly complementary to Imugene’s existing platform and portfolio.
  - Six patent families including composition of matter and method of use patents covering PD-1, Her-1, Her-2, Her-3, VEGF, IGF-1R, CD28 peptide vaccines and therapeutics.
  - Commercially attractive upfront payment; royalty rate in low single digit royalty on sales; exclusive, world-wide and sub-licensable until expiry of the last patent.

- Broadens and accelerates key Imugene Research and Clinical programs
  - PD-1 and HER2 + PD-1 combination programs accelerate by 24+ months
OSU WORLDWIDE, EXCLUSIVE LICENSE

- Six patent families, 22 patents
- IND ready PD-1 clinical trial (Phase 1)
- Ongoing Her-2 clinical trial (Phase 2)
- Six additional clinical candidates: Her-1, Her-2, Her-3, VEGF, IGF-1R CD28
- Three year R&D contract with access to Ohio translational labs

Access to experience and expertise with Prof. Pravin Kaumaya and team
WHY SELECT AND TARGET PD-1 FOR B-CELL VACCINATION?

Monoclonal antibody immunotherapies Keytruda® (Merck) and Opdivo® (BMS) targeting PD-1 sold USD$3.8B and $4.9B, respectively, in 2017.

Whilst acknowledging the rapid rise in clinical trials involving PD-1 and their combination with other treatments*, a PD-1 B-cell vaccination approach represents a paradigm shift in cancer immunotherapy.


In industry-recognized mouse cancer models (colon cancer), the PD-1 targeting B-cell vaccine is more superior than the gold standard mouse PD-1 monoclonal antibody (used in preclinical model testing for Keytruda and Opdivo).

The combination of the PD-1 vaccine with the acquired Phase II Her-2 vaccine significantly inhibits tumor growth c/w mAb control in a Her-2+ model of colon cancer.
PD-1/Her-2 vaccine combination active in model of colorectal cancer with no signs of toxicity

Inhibition of cancer growth 16 days after infusion of cancer cells

- All mice vaccinated over a period of 9 weeks showed no signs of scruffiness, lesions, and lethargy
- Organs (spleen, liver, heart, lung, kidney, and tumor) from the Balb/c mice vaccinated with combination peptides (HER-2 and PD-1) were collected from mice and submitted for analysis
- No significant lesions were noted in any of the organs submitted for histologic evaluation.
- There were also no overt biochemical abnormalities noted.
PD-1 “KEY-VAXX” VACCINE PHASE 1 DEVELOPMENT PATH 2018-2019

- **PD-1 candidate vaccine** identified May, 2018
- **CMC manufacturing**
- **Formal pre-clinical**
- **Finalise regulatory IND submissions**
- **2019: Commence Phase 1**

**Proposed Adaptive Phase 1/2 PD-1 Vaccine Design**

- **Dose Finding Signal Seeking**
  - Cohort 1
  - Cohort 2
  - Cohort 3

- **OBD**
  - **3-6**

- **Expansions Assumption**
  - *Safety*
  - *Immunogenecity*
  - *Tumor PD*

- **Expansion**

- **Indication Expansion (12-20 patients)**
  - **Proof of Concept**

- **Indication Expansion (12-20 patients)**
Combining drugs for better I/O outcomes is driving value creation presently.

Big Pharma are looking for novel combinations or “elusive blends” that:

- Combine without increasing toxicity
- Combine with minimal cost increase
- Combine for better response rates and efficacy

Imugene’s cancer vaccines potentially tick all three boxes.
Combination example

- July 2018, FDA approves Opdivo plus Yervoy combination for a certain subset of patients with metastatic colorectal cancer

- The FDA approval of combination Opdivo and Yervoy provides a novel therapeutic option with a higher response rate than that from monotherapy immunotherapy, **BUT**

- Unfortunately, more significant toxicity is noted with the combination, and diligence is needed to monitor these immune-mediated side effects

- Although early in development, Imugene’s PD-1 and Her-2 cancer vaccines potentially provide efficacy and response rate with minimal toxicity
The combination of different vaccine and therapeutic strategies to target specific molecular pathways that are dysregulated in tumors may create clinical breakthroughs for safe and efficacious cancer cures.

Today in the USA, over half a million cancer patients will die and the financial costs are exorbitant, running to over US$200 billion, a burden that is shared by patients and society as a whole. Unmet need across the cancer market is high, with most therapies conferring low levels of specificity and high toxicity. Therefore, there is a great need for innovative technologies that address these discrepancies. A potentially powerful line of defense against cancer that provides the opportunity to train the immune system to efficiently recognize and kill tumor cells would be highly significant in the field of personalized medicine. An ideal cancer treatment should be highly specific and have sufficient affinity to target systemic tumors at multiple sites in the body while discriminating between normal and cancerous cells. In this regard, antigen-specific cancer immunotherapy and immune targeting of the tumor neovasculature represent two attractive strategies for cancer prevention and treatment.

Molecular-targeted therapies provide marginal benefits. Immunotherapy in the form of antibodies and cytokines has become a fixture in our armamentarium of cancer treatments because of their potential as a safer and nontoxic alternative to present-day treatments. Many therapeutic modalities targeting receptor tyrosine kinases (RTKs) and downstream molecular pathways have been devised, and most outstanding among these are the EGF receptor (ErbB) and VEGF receptor (VEGFR) families [1–3]. Many agents include therapeutic antibodies to RTK ligands or the receptors themselves and small-molecule inhibitors that target the intracellular kinase domains of RTKs [4–6].

On the one hand, many of the blockbuster US FDA-approved monoclonal antibody (mAb) therapies targeting HER-2 (trastuzumab [Herceptin®; Genentech, CA, USA]), EGF receptor (cetuximab [Erbitux®; Imclone, NJ, USA]) and VEGF (bevacizumab [Avastin®; Genentech]) have significant toxicities, including cardiac dysfunction and congestive heart failure [7–9], and many patients on these drugs demonstrate disease progression due to development of resistance. Unfortunately, mAbs also suffer from a number of limitations including the frequency of treatments, associated costs, limited duration of action and undesired immunogenicity. On the other hand, clinically available small-molecule tyrosine kinase inhibitors (TKIs) include lapatinib (dual targeting EGF receptor and HER-2), sunitinib (targeting VEGFR1, VEGFR2, PDGF receptor [PDGFR], KIT and FLT3) and sorafenib (targeting VEGFR2, VEGFR3, Raf, PDGFR, KIT and RET). TKIs including sunitinib and sorafenib can cause toxicities in cancer patients. These inhibitors target multiple pathways including VEGFR, PDGFR and KIT. The toxicities associated with these TKIs may be due to the concomitant inhibition of several pathways. In addition, tumors eventually become resistant to TKIs in almost all treated patients. Furthermore, these drugs are
A TEAM WITH TRACK RECORD IN DRUG DEVELOPMENT

Leslie Chong (Sydney, Australia)
Managing Director & Chief Executive Officer
• Over 20 years of oncology experience in Phase I – III of clinical program development
• Leadership role involvement in two marketed oncology products
• Previously Senior Clinical Program Lead at Genentech, Inc., in San Francisco

Dr Axel Hoos (Philadelphia, U.S.A.)
Non-Executive Director
• Senior Vice President and Head of Oncology at GSK
• Former Medical Lead for Yervoy, the first survival improving medicine in Immuno-Oncology
• Chairman of the BoD of the Sabin Vaccine Institute
• Co-Chair of the Cancer Immunotherapy Consortium Think-Tank

Paul Hopper (Sydney, Australia)
Executive Chairman
• International & ASX biotech capital markets experience particularly in immuno-oncology & vaccines
• Former Chairman of Viralytics, Founder & Director of Prescient, Founder of Imugene & Polynoma LLC, former Director pSivida, Somnomed & Fibrocell Science

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

Dr Anthony Good (Sydney, Australia)
Vice President of Clinical Research
• Over 20 years global clinical development experience.
• Integral to the development of significant new medicines including Viagra, Revatio, Lipitor, and Somavert.
• Ex Pfizer Global Research and Development, Ex Covance Clinical Services.

Dr Mark Marino (San Diego, U.S.A.)
Chief Medical Officer
• Leads the Company’s global clinical development, regulatory and medical monitoring activities
• Previously held CMO positions at Daiichi-Sankyo, Hoffman-La Roche AG, and Novartis
• Dr Marino holds a Medical Doctor degree from the Albert Einstein College of Medicine
Our competition is cancer, and in that fight, we’re collaborating with an outstanding team of medical researchers and oncologists.
FINANCIAL SUMMARY

ASX: IMU

Options on issue (as at July 2018)

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<th>No. of options</th>
<th>Exercise Price</th>
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<td>$0.026</td>
<td>30/11/2020</td>
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<td>Listed: (IMUOB)</td>
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<td>Total:</td>
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<td>$0.03*</td>
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Top 5 shareholders (as at July 2018)

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<th>No. of Shares</th>
<th>% Capital</th>
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<tr>
<td>National Nominees Limited</td>
<td>240,906,746</td>
<td>6.69%</td>
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<td>HSBC Custody Nominees Limited</td>
<td>165,986,536</td>
<td>4.61%</td>
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<td>Dr. Nicholas Smith</td>
<td>86,000,000</td>
<td>2.39%</td>
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<td>J P Morgan Nominees Australia Limited</td>
<td>79,957,741</td>
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<tr>
<td>Paul Hopper Executive Chairman</td>
<td>75,678,722</td>
<td>2.10%</td>
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Market Cap (31/Jul/18): $79.2M AUD, $58.9M USD

Ordinary Shares: 3.559 billion

12 month price range: 1.3 cents – 3.9 cents AUD

Avg daily volume: 9.5M shares (April-July 2018)

Investment to Date: ~$42.5M (public)
~$5.5M (VC)

Cash & Equivalents: $25.8M (as at 31 July 2018)
EXECUTIVE SUMMARY

• **Imugene B-cell vaccine pipeline**: Broadened and strengthened clinical programs globally, brings the Imugene platform and technology into **US and European focused clinical trials**

• **Synergistic technology acquisition from Ohio State University and The Mayo Clinic**: Full spectrum of indications and targets to choose from, including check point inhibitors and combination therapies. **Accelerates** and advances Imugene PD-1 vaccine program by **24 months**

• **Experienced management & board**: Meeting milestones and successful M&A activity