Imugene Limited – Receives Orphan Drug Designation for Bile Tract Cancer Therapy and Reports Encouraging Blood Cancer Trial Outcomes

Imugene Ltd. (ASX: IMU)

IMUGENE
Developing Cancer Immunotherapies

Share Price: A$0.049	Valuation: A$0.49

Key Statistics

52 Week Range	A$0.039 - A$0.150
Avg. Volume (3 months)	21.13M
Shares Outstanding	7.44B
Market Capitalization	A$370.98M
EV/Revenue	N/A
Cash Balance*	A$93.11M
Analyst Coverage	3

***Cash balance as of June 2024**

Revenue (in A$mm)

June - FY	2023	2024E	2025E
1H	N/A	N/A	N/A
2H	N/A	N/A	N/A
FY	N/A	N/A	N/A

EPS (in A$)

June – FY	2023A	2024E	2025E
1H	(0.00)	(0.01)	(0.01)
2H	(0.00)	(0.01)	(0.01)
FY	(0.01)	(0.02)	(0.02)

Stock Price Chart (in A$)

Investment Highlights

- **Imugene Receives Orphan Drug Designation for Bile Tract Cancer Therapy -** Imugene Limited has been granted Orphan Drug Designation (ODD) by the U.S. FDA for its oncolytic virotherapy, CF33-hNIS (VAXINIA) for the treatment of cholangiocarcinoma, a rare and aggressive form of bile tract cancer. This designation, aimed at promoting treatments for rare diseases, grants Imugene incentives such as tax credits, fee waivers, and seven years of market exclusivity upon approval. The decision follows promising results from the Phase 1 MAST trial, where VAXINIA demonstrated encouraging efficacy, including one patient achieving a complete response. Imugene has since expanded the trial to include 10 additional patients with bile tract cancers. These developments strengthen Imugene's position as a leader in immuno-oncology, driving innovation in treatments for rare cancers with high unmet clinical needs.

- **Significant Advances in Blood Cancer Treatment Evidenced by Imugene's azer-cel CAR T Trial Results -** Imugene Limited reported promising outcomes from its Phase 1b clinical trial of azer-cel (azercabtagene zapreleucel), an allogeneic CD19 CAR T therapy, in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL). The trial included 10 patients treated to date, with six in Cohort A receiving azer-cel and lymphodepletion and four in Cohort B receiving the same treatment plus interleukin 2 (IL-2). Notably, three patients achieved complete responses, two from Cohort B and one from Cohort A, with those in Cohort B demonstrating sustained remission for over 90 days and 120 days. The trial's Cohort B, which includes a small dose of interleukin 2 (IL-2), has shown promising results in prolonging the survival of modified T-cells, which are crucial for effectively targeting and destroying cancer cells. This adjustment aims to increase both the response rate and the longevity of the treatment's effectiveness. With these early encouraging outcomes, Imugene is planning to acquire more data, particularly looking for biomarkers that indicate the treatment's improved performance. The company is set to continue enrolling patients in Cohort B, aiming to compile a robust data set for a potential Phase 2/3 trial submission to the FDA. All participants in Cohort B had previously not responded to several lines of treatment, including autologous CAR T therapies, and they continue to participate in the trial, showing the regimen's potential for durable responses. The study, conducted at numerous prestigious cancer centers in the U.S. and soon to expand to Australian sites, has demonstrated acceptable safety and tolerability of the treatment. Building on these substantial achievements, Imugene is expected to advance into broader clinical trials, potentially setting new standards for the treatment of blood cancers with its innovative azer-cel therapy.

Company Description

Imugene Limited is an Australian clinical-stage immuno-oncology company developing a range of immunotherapies to activate the immune system of cancer patients to treat and eradicate tumors. The company is developing six unique assets targeting multiple forms of solid tumors and hematologic malignancies.

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Company Overview

Imugene Limited (ASX: IMU) is an Australia-based clinical-stage biotechnology company focusing on developing immunotherapies for the treatment of various cancers. The company has a diversified pipeline of 5 unique assets developed on a strong research base of 4 platform technologies. The company is targeting ten disease areas with high unmet needs and low survival rates. Imugene's initial focus has been to advance its B-cell peptide vaccines technology, which stimulates the body's immune system to produce antibodies against the normal self-proteins, such as HER2 and PD-1. The two lead therapies within the company's pipeline include HER-Vaxx and PD1-Vaxx, aimed at treating Gastric, and Non-Small Cell Lung Cancer and Colorectal Cancer, respectively. Expanding its purview, the company acquired the exclusive license to the CF33 Oncolytic Virus technology developed by Professor Yuman Fong at the City of Hope (COH) Cancer Centre in Los Angeles. CF33 is a novel, genetically engineered chimeric orthopoxvirus and has shown promising efficacy in a range of mouse models. Clinical development of CF33 oncolytic virus is being studied in two different constructs, CHECKvacc (CF33+hNIS+anti-PD-LI) and VAXINIA (CF33+hNIS). Both constructs are currently being pursued under phase 1 clinical trial. In addition to B-cell immunotherapy and CF33, Imugene, in May 2021, obtained the worldwide exclusive licenses to the patents covering CF33-CD19, also known as onCARlytics. The CF33-CD19 agent aid CD19-directed CAR T by labeling cancer cells for CAR T cell destruction. CD19 CAR T as a monotherapy faces key challenges in solid tumors largely due to a lack of selectively and highly expressed surface antigens. Furthermore, the company is also developing Azer-cel as a Potential First-in Class Allogeneic CAR T Product Candidate for CD19+ CAR T Relapsed Patients.

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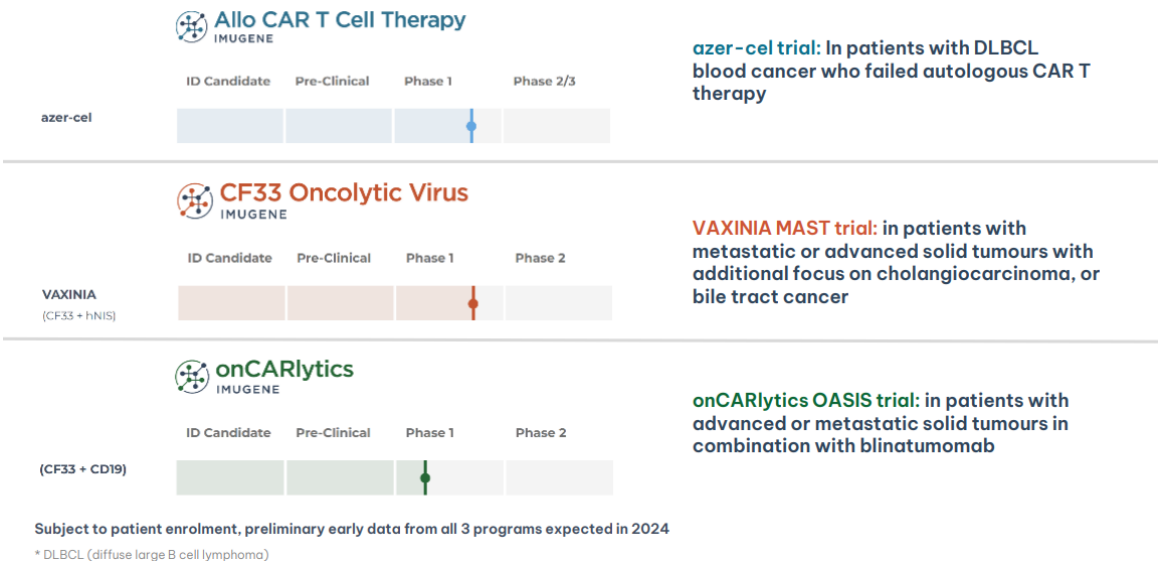

Exhibit 1: Imugene's Immunotherapy Pipeline Assets. Source: Company Presentation

Imugene's platform technology IP is protected by a set of patents, with a majority of the patent expiration starting post-2035. In order to advance its pipeline through different clinical stages and commercialization, the company has signed a clinical trial supply agreement with pharmaceutical giants Roche (SWX: ROG), and Merck KGaA (ETR: MRK), adding further validation to its pipeline candidates. The company's pipeline indication represents a multi-billion-dollar market opportunity targeting the highly valuable market of cancer immunotherapy.

Allogeneic CAR T Cell Therapy

Allogeneic CAR T cell therapy is an innovative approach in the field of cancer immunotherapy, where T cells from a healthy donor are genetically engineered to fight cancer cells in patients. This method is a form of adoptive cell transfer, designed to harness the power of the immune system to target and destroy cancer cells. Allogeneic CAR T cell therapies are currently under clinical trials and are not yet widely available as standard treatments. These therapies hold significant promise due to their potential to broaden the accessibility of CAR T cell therapies to more patients, offering a quicker and potentially more cost-effective treatment option compared to their autologous counterparts.

In CAR T cell therapy, T cells—a type of white blood cell crucial for immune responses—are collected from a donor. These cells are then genetically modified in a laboratory to express a chimeric antigen receptor (CAR) on their surface. The CAR is specifically designed to recognize and bind to antigens on the surface of cancer cells. Once the CAR T cells are infused back into the patient's body, they seek out and bind to the cancer cells through the specific antigens. Upon binding, the CAR T cells are activated and then proliferate, kill the targeted cancer cells, and potentially persist in the body to provide ongoing surveillance against the cancer.

Benefits of Allogeneic CAR T Cell Therapy

1. Off-the-Shelf Availability: Allogeneic therapy uses cells from a healthy donor, allowing the cells to be prepared in advance and stored, ready for use as an "off-the-shelf" treatment. This contrasts with autologous CAR T cell therapies, where cells are taken from the patient, requiring a bespoke production process for each individual.

2. Broader Reach and Lower Cost: Since the therapy does not require individualized cell harvesting and processing for each patient, it can potentially be more cost-effective and accessible to a wider range of patients.

Azer-cel – Allogeneic CAR T Candidate for CD19+ CAR T Relapsed Patients

The company's acquisition of Precision Biosciences' allogeneic CAR T cell therapy, azer-cel is another major addition to its pipeline that complements Imugene's onCARlytics program. While azer-cel continues to progress for r/r NHL patients in clinical trials, the acquisition allows Imugene to develop its own combination solution in multiple hard-to-treat solid tumor indications. This enables the company to streamline R&D, manufacturing, marketing, and distribution processes, eliminating reliance on third parties, potentially leading to significant cost savings to market. Azer-cel therapy has demonstrated robust and compelling efficacy and safety data from its phase 1 trial that included 84 patients with non-Hodgkin's Lymphoma (NHL) (n=61) and B-cell Acute Lymphoblastic Leukemia (B-ALL) (n=23). Azer-cel has demonstrated high response rates and a tolerable safety profile in relapsed /refractory NHL patients. Among all evaluated subjects (n=61), the overall response rate (ORR) was 58%, with 41% achieving a complete response (CR). The response was particularly promising among NHL patients who had relapsed following autologous CAR T therapy (n=18), reporting an ORR of 83% and a CR of 61%, with 55% maintaining their response for six months or more. No severe cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), infection, or graft versus host disease was observed. Azer-cel's encouraging results highlight its potential to improve patient outcomes, particularly for those patients who have relapsed after being treated with auto CAR T therapy. The company has also been engaged in efforts to improve the therapeutic index of the novel allogeneic

CAR T therapy by optimizing the total fludarabine exposure during lymphodepletion to increase CAR-T cell expansion and improving the manufacturing processes to improve CAR T cells' fitness and reduce potential inflammatory toxicities.

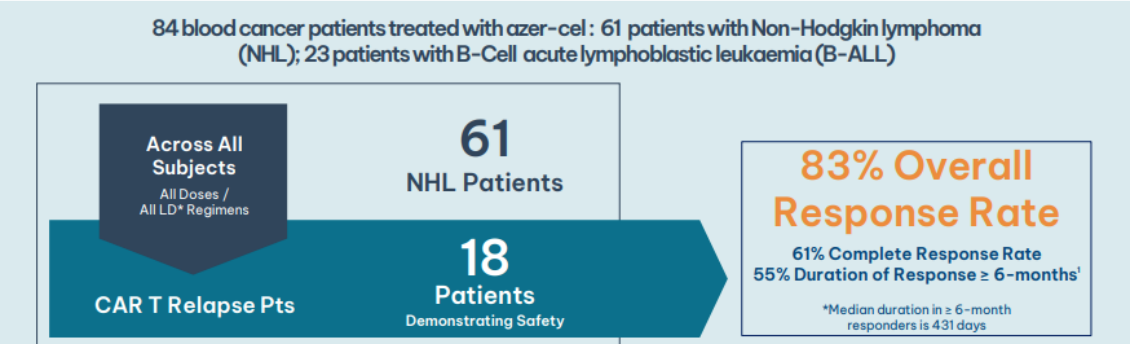

Exhibit 2: Azer-cel High Response Rates and Durability. Source: Company Presentation

Non-Hodgkin Lymphoma (NHL) is one of the most prevalent cancers in the United States, making up approximately 4% of all cancer diagnoses. In 2023, the American Cancer Society estimates that about 80,550 individuals, encompassing both children and adults, will be diagnosed with NHL, and about 20,180 individuals will succumb to this cancer in the same year. For early-stage NHL, localized radiation therapy or a combination of radiation and chemotherapy may be used. For more advanced stages, a combination of chemotherapy and immunotherapy is often the first-line treatment regimen. The second and further line of treatment includes salvage chemotherapy, stem cell transplant, targeted drugs, and immunotherapy (such as CAR-T cell therapy). The first-line treatment options are found to be inadequate, with a relapse/refractory rate of 30-40% in patients with Diffuse large B-cell lymphoma (DLBCL), the most common sub-type of NHL. The salvage chemotherapy proceeded with stem cell transplantation, a common second-line treatment regimen has also shown modest success, with relapse occurring in 30-50% of the patients. Further line treatment options include FDA-approved autologous CAR-T therapies; it is estimated that 60-70% of patients will likely relapse, with 85% of relapsed patients continuing to express CD19 protein. Azer-cel holds multiple advantages compared to FDA-approved CAR-T therapies and thus has the potential to be the preferred treatment option for patients who are refractory or have relapsed post-second-line treatment regimen.

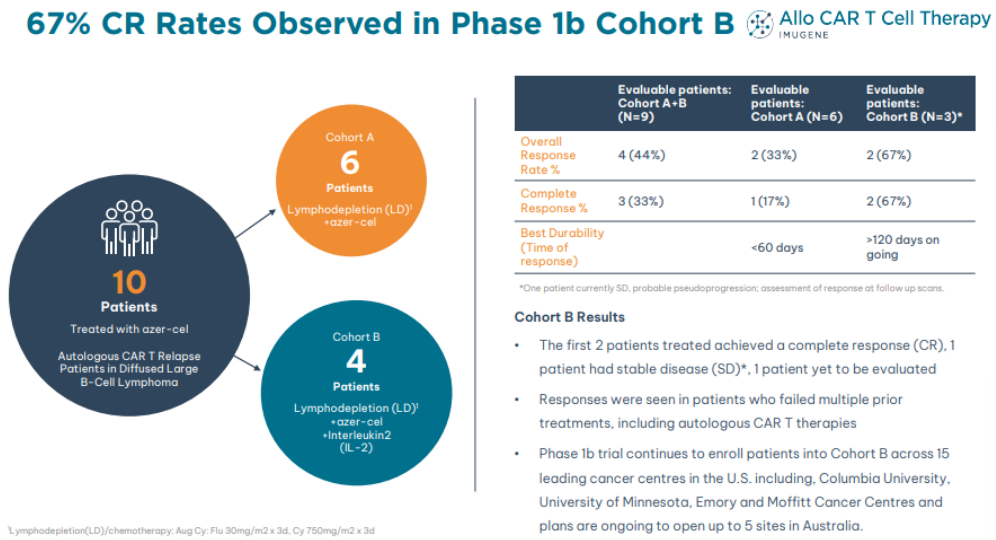

Exhibit 3: Azer-cel Phase 1b Clinical Results. Source: Company Presentation

Precision has previously concluded an end-of-Phase 1 meeting with the U.S. FDA aimed to gain further understanding of the potential registration path for azer-cel. Encouraging feedback has been received, providing a pathway towards registration. A Phase 2 pivotal study in the U.S. will likely be undertaken post the completion of the Phase 1b study, with the potential for rapid advancement to regulatory filings. The phase 1b study has so far demonstrated promising outcomes in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL). The trial included 10 patients treated to date, with six in Cohort A receiving azer-cel and lymphodepletion and four in Cohort B receiving the same treatment plus interleukin 2 (IL-2). Notably, three patients achieved complete responses, two from Cohort B and one from Cohort A, with those in Cohort B demonstrating sustained remission for over 90 days and 120 days.

Oncolytic Virus - An Emerging Frontier in Cancer Immunotherapy

A virus is an infectious agent that utilizes the host's genetic material to replicate itself, thereby spreading to healthy cells. One such substrate of naturally occurring or genetically modified viruses that act as a potent therapeutic agent and have the ability to infect and kill cancer cells are commonly called Oncolytic viruses. Cancer cells have impaired anti-viral defenses and are susceptible to infections. Modification in Oncolytic viruses through genetic engineering enhances their ability to deliver therapeutic payload and diminishes the possibility of widespread resistance.

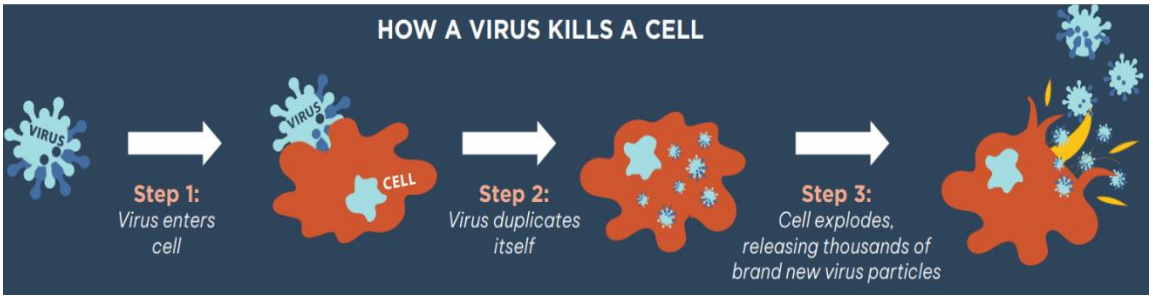

Exhibit 4: Oncolytic Virus Mechanism of Action. Source: Imugene Limited

Although oncolytic viruses are potentially powerful therapeutic agents for cancer treatment, a single type of oncolytic virus is not enough to destroy all the cancer cells due to the heterogeneity of cancer tissues and the complexity of cancer cells. Determining the virus and delivery method are two of the most challenging and crucial parts of the underlying therapy.

Developed at the City of Hope Cancer Center in Los Angeles, California, CF33 is a chimeric vaccinia virus derived from genomic sequencing of multiple strains of vaccinia virus, thus generating a safer and more potent virus that is also immunostimulatory. Nine different “parental” virus strains of orthopoxvirus (cowpox virus, rabbitpox virus, raccoon pox virus) were introduced, grown, and titered in CV-1 cell lines leading to the creation of 100 chimeric orthopoxviruses. These “daughter” virus strains contained different combinations of genes from the parental virus, which were then tested for potency by screening them against the NCI-60 panel. CF33 proved to be the most potent and is chosen further for in vivo and clinical development.

VAXINIA (CF33 + hNIS)

CF33 with Human Sodium-Iodide Symporter (hNIS) gene is currently being evaluated in the phase 1 Mixed Advanced Solid Tumors (MAST) study. Encoding of hNIS gene enables reliable non-imaging of viral replication using positron emission tomography mediating targeted radiotherapy. CF33 encoded hNIS gene has been previously studied in colon cancer xenograft mouse model, demonstrating the synergy of oncolytic viral therapy with radioablation in vivo.

The cancer cell lines induced xenografts were implanted into athymic nude female mice and were administered with either intratumoral PBS or CF33-hNIS injections. CF33-hNIS-induced tumor growth abrogation and regression were observed in animals with HCT116-derived xenografts. Abrogation and regression of tumor growth were also observed in HT29-derived tumors in some mice, but the results were not statistically significant. Additionally, the treatment was found synergistic with I-131 Radioisotope, exhibiting an effective and sustained tumor growth inhibition when compared to monotherapy treatment with PBS, CF33-hNIS, or I-131. The use of a more targeted approach (CF33 + hNIS + I-131) would decrease toxicity and enhance efficacy at a lower dosage and cost.

Oncolytic Virus Market and Competitive Overview

Oncolytic virus as a treatment modality has gained a lot of attention after positive results from many clinical trials. The ability to infect cancer cells selectively while allowing for additional genetic modification and stimulating the innate immune system to fight cancer cells offers a novel approach to cancer immunotherapy. The most notable shift in the OV field has been from its application as a direct lytic agent to its development as a multimodal agent involving cell lysis, immune stimulation, and gene therapy, which further established OV as a strong candidate for cancer therapy.[1]

There are 162 Oncolytic virus therapy currently under active development as of June 2022, of which only four have successfully navigated through clinical development and received regulatory approval. 63% or 103 therapies are in the early stages and haven't even progressed through clinical trials. Of the four OV therapies that have been approved, Imlygic (talimogene laherparepvec) is the most noteworthy, being studied across 50 clinical trials. It was approved for the treatment of melanoma in 2015 by the FDA and EMA. Other OV therapy approval relates to comparatively smaller pharmaceutical markets.

onCARlytics - 'Mark and Kill' Approach

Expanding the Immuno-oncology portfolio, the company licensed the CD19 Oncolytic virus from City of Hope, enabling CD19 CAR-T against solid tumors. CD19-directed CAR T as monotherapy has shown remarkable success in hematological malignancies, but its applicability in solid tumors is accompanied by various challenges which have led to poor outcomes in pre-clinical and clinical studies. Antigen escape, toxicity related to CAR-T cells, antigen heterogeneity, the trafficking of CAR-T cells and tumor infiltration, poor stability, and immunosuppressive microenvironment are among the limitations that impede the ability of CAR-T cell therapy to produce sustained response in patients with solid malignancies (accounts for 90% of all cancer cases worldwide).

Higher generation CAR-T therapy has been shown to have superior ant-tumor activity when compared to first and second generations therapies. However, even with the use of a high later generation of CAR T-cells products, objective responses for trials in solid tumors have been mostly disappointing. Many studies are focusing on enhancing the applicability and usefulness of CAR-T therapies by combining it with other adjuvant therapies. One such combination therapy where Imugene believes that the combination can yield promising results is the use of Oncolytic virotherapy with CD19-directed CAR-T therapy. OVs' ability to selectively replicate themselves while developing adaptive anti-tumor immunity has gained a lot of attention since the FDA approval of T-VEC. OVs can also be engineered in such a way that forces the expression of certain

[1] Cancers 2021, 13(21), 5452; https://doi.org/10.3390/cancers13215452

genes in the tumor milieu, that is, activating the targeted transgenic delivery potential, thus augmenting the oncolytic viral treatment.

The company is leveraging the transgenic delivery mechanism of Oncolytic Viruses such as CF33 to infect cancer cells and encourage the selective expression of a CAR-targetable tumor antigen, a truncated non-signalling variant of CD19 (CD19t). These underlying mechanisms of OVs allow endogenous production of T-cells and CAR T-cell infiltration into tumors, eventually exhibiting cancer-killing activities. Imugene obtained the worldwide licenses of the patents covering the cell therapy technology, which includes CF33-CD19, known as onCARlytics™, developed at City of Hope.

B-Cell Peptide Cancer Vaccines - An Effective Active Immunization Approach

In the past decade, there have been considerable advancements in cancer treatment, with targeted therapies and immunotherapies showing great promise for multiple types of cancer. Passive immunization, such as the use of humanized monoclonal antibodies, is proven to have promising therapeutic applications in the treatment of different forms of malignancies but comes with several caveats that limit the usage of these therapies in numerous cases. Toxicity problems and resistance, high costs, sophisticated therapeutic regimen, and long half-life are a few of the significant shortcomings that have raised the need for an efficacious and long-lasting active immunization approach. One such approach that Imugene believes can cause a paradigm shift in cancer research is the advancement of B-cell epitope vaccines. Cancer vaccines based on B-cell peptides are generally composed of an adjuvant and an immunogenic protein containing a B-cell epitope peptide that can induce B cells to create polyclonal antibodies that bind to different parts of the vaccine antigens. The resulting construct of polyclonal antibodies yields a powerful antitumor effect that is long-lasting and inhibits tumor recurrence. Even though humanized mAbs have a somewhat similar mechanism of action, the use of synthetic bodies to treat cancer has been fraught with several concerns. Poor penetration across tissues, large quantities of hmAbs resulting in toxicity, expensive treatment (average cost: US$150,000 per year), and long and frequent infusions. Despite these challenges, hmAbs therapy has become a multi-billion-dollar business.

The use of B-cell immunotherapies to stimulate the patient's immune system to produce polyclonal antibodies may have advantages over synthetic antibodies

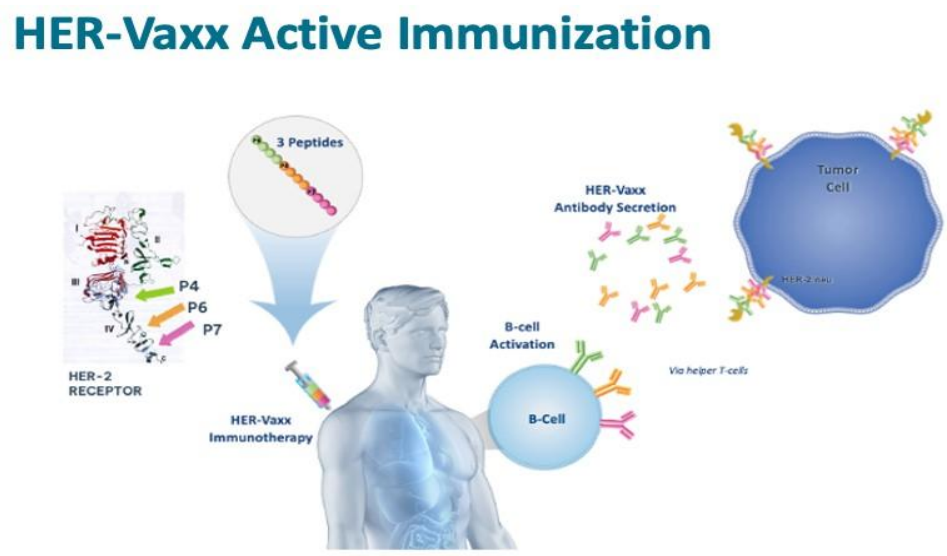

Exhibit 5: B-Cell Epitope Peptide Vaccine Mechanism of Action. Source: Imugene Limited

HER-Vaxx – Cancer Vaccine for Gastric Cancer

HER-Vaxx is B-cell immunotherapy that is designed to treat cancers that overexpresses HER2 protein. Different types of solid tumors such as breast cancer, gastric cancer, ovary, endometrium, bladder, head, and neck cancer have been found with over-expression of the HER2 protein. The amplification/over-expression is often associated with poor prognosis and low survival rates. HER-Vaxx is a B-cell peptide vaccine composed of 3 fused epitopes (p467) derived from the extracellular domain of HER2/neu coupled to CRM197 and adjuvanted with Montanide.[2] The resultant vaccine formulation induces a potent polyclonal antibody response that targets cells with overexpressing HER-2 receptors on their surface. Pre-clinical studies have shown strong anti-tumor activity in-vitro and in-vivo and better growth inhibition of breast cancer cells or HER2 signaling pathway compared with single-agent mAb trastuzumab.

HER-Vaxx has been shown to stimulate a potent polyclonal anti-body response to HER-2/neu, a well-known and validated cancer target

The current vaccine formulation is an enhanced version that replaces virosomes used in previous formulations of HER-Vaxx. The company had previously examined the virosomal formulation in phase 1 clinical trial in end-stage breast cancer patients. While the study showed good immunogenicity as well as an excellent safety profile, several drawbacks of the virosomal formulations, including solubility and limited stability after coupling all the single peptides together to virosomes, were the reasons to reconstruct and improve the multi-peptide vaccine with respect to specificity and clinical applicability. The enhanced formulation has been shown to have a faster production of antibodies and a more rapid immune response.

Competitive Overview

Imugene's lead drug candidate HER-Vaxx faces competition from already approved HER2-directed gastric cancer mAbs and PD-1 binding immune checkpoint inhibitors. Multiple targeted therapies and immunotherapies are currently under clinical trial for advanced or metastatic gastric cancer, indicating fierce competition in this particular disease area. Trastuzumab (Herceptin) and fam-trastuzumab deruxtecan-nxki (Enhertu) are major HER-2-directed therapeutics that are FDA-approved. Even though HER-Vaxx exhibited robust efficacy and safety in the early stages of clinical development, the company's ability to fend off competition depends on its superior safety and comparative efficacy profile at a reasonable cost.

Drug	Patent expiry	Annual Revenue (2021)	Pricing
Trastuzumab	off-patent	$2,694 million	$76,500
nivolumab	2028	$7,523 million	$187,728
fam-trastuzumab deruxtecan-nxki	2024	$426 million	$164,000

Exhibit 6: Major FDA-approved Gastric Cancer Drugs. Source: Diamond Equity Research, Company Filings

PD1 – Vaxx – Therapeutic Vaccine for NSCLC

Immune Checkpoint Inhibitors as potent immunotherapy has already reached consensus, with numerous FDA approvals for several cancer types recording billions of dollars in sales worldwide. Thousands of immunotherapies are currently being tested in clinical trials for different types of malignancies. Even though PD-1/PD-L1 signaling inhibitors have shown great clinical success,

Constructed from a single B cell epitope derived from extracellular domain of PD-1, PD-1 Vaxx has shown great potential in pre-clinical and early-stage clinical trials

[2] Future Oncology 2020 16:23, 1767-1791

the development of primary and secondary resistance has contributed to just a small subset of patients (10–15%) responding to the monotherapy.[3]

PD-1 Vaxx is potentially a cost-effective, potent, and novel approach toward inhibiting the PD1/PD-L1 signaling pathway, thus triggering anti-cancer effects similar to those observed in ICI mAbs such as Keytruda® and Opdivo®. Based on the B-cell epitope peptide vaccine platform technology, PD-1 B-cell peptide epitope vaccine (PD-1 Vaxx) is derived from extracellular amino acids 92-110 of PD-1 linked to a measles virus fusion peptide (MVF) amino acid 288-302 via a four amino acid residue (GPSL). The resulting formulation, when injected, elicits a B-cell antibody response, inducing the body to produce polyclonal antibodies. These antibodies block the PD-1 signaling pathway that is crucial for tumor growth and simultaneously promotes T-cell recognition of cancer cell leading to targeted killing. Activation of both T-cell and B-cell functioning encourages immunological response providing a formidable cancer immunotherapy candidate.

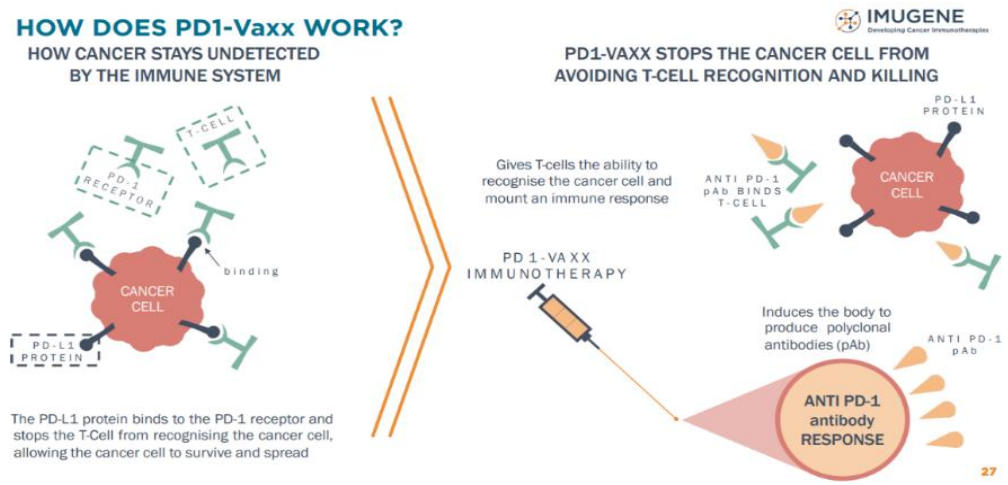

Exhibit 7: PD-1 Vaxx Mechanism of Action. Source: Imugene Limited

PD1-Vaxx for Colorectal Cancer

Imugene is initiating a Phase 2 trial, named "Neo-POLEM," in the UK and Australia, focusing on PD1-Vaxx for patients diagnosed with operable colorectal cancer (CRC). This trial, supported by various cancer research groups, aims to evaluate the vaccine's effectiveness in reducing tumor burden before surgery in CRC patients, particularly those with a specific genetic feature (dMMR/MSI-H). The study will enroll around 44 patients over 18 months. It's a significant step in exploring novel treatments for CRC, a common and often deadly cancer, using innovative immunotherapy approaches. Additionally, Imugene has received a notification of intent from the European Patent Office about granting a patent for PD1-Vaxx. The patent, expiring in 2038, encompasses the manufacturing and treatment methodology of PD1-Vaxx.

Colorectal cancer (CRC), also referred to as bowel cancer, ranks as the third most prevalent cancer globally, recording over 1.2 million new cases annually and a mortality rate close to 50%. Approximately 80% of colon cancer cases are local and can be surgically removed at the time of diagnosis. In 2018, Australia registered 15,610 new instances of bowel cancer (8,490 in males and 7,120 in females). By 2022, the estimates indicated 15,713 new diagnoses in Australia (8,300 males and 7,413 females). The likelihood of being diagnosed with bowel cancer by age 85 is

[3] British Journal of Cancer (2021) 125:152–154

approximately 1 in 19 (5.2%), with a slightly higher risk for males (1 in 18 or 5.6%) compared to females (1 in 21 or 4.8%). The primary treatment for locally advanced colorectal cancer involves neoadjuvant (pre-surgical) chemotherapy followed by the surgical removal of the affected colon or rectum. A specific group of colorectal cancers, characterized by a deficiency in "mismatch repair" (dMMR) and known as microsatellite instability (MSI), leads to higher mutation rates in cancer cells and accelerated tumor growth. Given that dMMR colorectal cancers respond well to programmed death 1 (PD-1) blockade when metastatic, it's proposed that PD1-Vaxx checkpoint blockade could be effective for those with mismatch repair-deficient, locally advanced colorectal cancer.

Key Risks

- **Clinical Development Risk -** Imugene's market value is tied to its therapeutic products currently in clinical trials. Failure to deliver satisfactory efficacy and safety profile or statistically significant results could negatively impact the company's value.

- **Regulatory Risk -** Post successful completion of clinical trials, the company is required to gain regulatory approval from foreign and or domestic regulatory bodies. Failure to obtain regulatory approval in any of the targeted geographies could negatively impact the company's addressable market and, therefore, the overall value of the company.

- **Foreign Exchange Risk -** The company is exposed to foreign exchange risk, given that clinical trials and other research activities are carried out in foreign geographies. Wide fluctuations in foreign currency could impact the company's cost profile and cash burn.

- **Financing and Dilution Risk -** Imugene is a pre-revenue biotechnology company and relies on external sources of financing to progress its pipeline. Failure or delays in obtaining the required capital would hinder the company's operating and research activities, leading to deferment in expected clinical and approval timelines. Financing capital by issuing further equity will dilute the shareholding of existing shareholders.

- **Competitive Risk -** The cancer Immunotherapy market has expanded in the past decade with multiple approvals and thousands of therapeutic products currently in clinical trials. Imugene faces competition from many of the therapeutic products being evaluated in clinical trials, which might affect the company's ability to position and gain market share in its targeted geographies.

These risk factors are not comprehensive. For a full list of risk factors, please read Imugene's latest prospectus and/or annual filings.

Appendix

Income Statement	FY2022 A	FY2023 A	FY2024 E	FY2025 E	FY2026 E
Net sales	-	-	-	-	87,567,258.3
Cost of sales	-	-	-	-	(17,513,451.7)
Gross profit	**-**	**-**	**-**	**-**	**70,053,806.6**
Operating expenses					
General and Administrative Expenses	(14,061,251.0)	(20,428,456.0)	(62,246,886.2)	(73,591,860.1)	(76,490,921.2)
Marketing Expense	-	-	-	-	-
Research and Development	(36,611,892.0)	(30,864,770.0)	(79,133,734.9)	(87,297,108.4)	(67,104,015.1)
Operating Loss	**(50,673,143.0)**	**(51,293,226.0)**	**(141,380,621.1)**	**(160,888,968.6)**	**(73,541,129.7)**
Other income/ (expense)					
Research and development tax incentive	12,614,130.0	11,741,527.0	21,643,920.0	23,937,954.8	9,851,316.6
Other grants	-	-	-	-	-
Other gains/(losses) - net	117,914.0	(215,540.0)	-	-	-
Finance income	192,249.0	1,879,802.0	3,828,766.6	1,807,161.9	286,584.6
Finance expense	(120,324.0)	(27,453.0)	(265,407.0)	-	-
Profit before exceptional items, extraordinary items and tax	**(37,869,174.0)**	**(37,914,890.0)**	**(116,173,341.6)**	**(135,143,851.9)**	**(63,403,228.6)**
Exchange loss (net)	-	-	-	-	-
Employee seperation cost	-	-	-	-	-
Profit before tax from continuing operations	**(37,869,174.0)**	**(37,914,890.0)**	**(116,173,341.6)**	**(135,143,851.9)**	**(63,403,228.6)**
Income tax (expense) benefit	-	-	-	-	-
Net earnings including noncontrolling interests	**(37,869,174.0)**	**(37,914,890.0)**	**(116,173,341.6)**	**(135,143,851.9)**	**(63,403,228.6)**

Exhibit 8: Income Statement (in A$). Source: Diamond Equity Research

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