patrys

ANNUAL REPORT 2020 (EXTRACT)

Contents

From the Chairman

To our valued shareholders and supporters,

I would like to again extend my gratitude for your ongoing support of our business this year.

At a time of considerable global uncertainty and heartache due to the Coronavirus (COVID-19) pandemic, we have managed to lean into our community of academic and commercial partners to facilitate valuable progress in our research and development (R&D).

I am enormously proud of the work we have undertaken to develop our Deoxymab platform. Earlier this year Patrys' research collaborators from Yale School of Medicine, Dr James Hansen and Dr Jiangbing Zhou, gained insights into the unique mechanism of action of our lead candidates PAT-DX1 and PAT-DX1-NP, revealing how these novel antibodies can potentially target aggressive cancers.

We now know that PAT-DX1 exploits the DNA Damage Response (DDR) mechanism to block DNA repair and preferentially kill cancer cells. In animal models, it has shown efficacy in killing cancer cells with a range of DDR gene mutations. Unlike other known antibodies and 98% of small molecules, it can also cross the blood brain barrier (BBB) to access cancer cells in the central nervous system.

Our research collaborators in the US and Australia have been successful in obtaining multiple prestigious grants to the value of US$3.13m (A$4.87m) over the next five years to progress this work. This is a significant endorsement of their discoveries to date and an important commercial and reputational boost for our Company too.

We look forward to progressing our development programs with the intention of working towards finalising stable cell line development this calendar year, completing toxicology studies in the new year and filing for a clinical trial in late 2021 or early 2022. With the PAT-DX1 development program on track and progressing well we will also start to broaden the range of platform applications for the Deoxymab technology, including investigating alternate formats of the antibody and expanding our efforts on nanoparticle conjugation. This will ensure that the Company has both breadth and depth in its development portfolio, and position us well for business development discussions.

Thank you once again for your support and we look forward to another productive and rewarding year ahead.

John Read

Patrys Chairman

"We are dedicated to improving the health and quality of life of those diagnosed with aggressive forms of cancer with our novel Deoxymab platform."

- Patrys Chairman, John Read

Patrys people

Patrys has attracted respected global leaders in clinical research, pharmaceutical development, and commercialisation. We have a lean, multidisciplinary team, committed to maintaining the highest standards in research and development.

Board of Directors

John Read, BSc (Hons), MBA, FAICD
Chairman

Mr Read is an experienced Chairman and Director in public, private and government organisations. Through his extensive career in venture capital, private equity and commercialisation he has gained a depth of experience in the formation and growth of emerging companies with an emphasis on commercial entities that provide broad societal benefits.

James Campbell, BSc (Hons), PhD, MBA, GAICD
Chief Executive Officer and Managing Director

Dr Campbell has more than 20 years of international biotechnology research, management and leadership experience and has been involved in the creation and/or transformation of multiple successful Australian and international biotechnology companies.

Michael Stork, BBA
Non-Executive Director

Mr Stork is the Managing Director of Stork Holdings Ltd, an investment company active in the Canadian technology start-up sector. Mr Stork is active on the Boards of a number of leading Canadian technology companies and other institutions.

Suzy Jones
Non-Executive Director

Ms Jones is Founder and Managing Partner of DNA Ink LLC, a life sciences advisory firm in San Francisco with clients in the United States and Europe. Ms. Jones has extensive networks within the pharmaceutical and biotech companies and venture capital community in North America.

Pamela M. Klein, BSc, MD
Non-Executive Director

Dr. Pamela M. Klein completed her medical training at Stritch School of Medicine, Loyola University in Chicago, followed by internal medicine training at Cedars-Sinai, Los Angeles, prior to spending 7 years working at the U.S. National Cancer Institute. Dr. Klein then moved to Genentech where, as Vice President, Development she led the development of a large portfolio of drugs including Herceptin, Tarceva and Perjeta. More recently Dr. Klein has held a range of executive, advisory and board positions including the board of Argenx (Euronext and NASDAQ).

Scientific Advisory Board

Allen Ebens, BSc, PhD

Dr Allen Ebens completed a PhD at UCLA and Post-doctoral training at UCSF. Over 20 years his distinguished career has seen significant contributions to the scientific literature as well as advancement of five discovery projects to clinical development at companies including Exelixis, Genentech and Juno Therapeutics.

Peter Ordentlich, BSc, PhD

Dr Peter Ordentlich completed a PhD in Immunology at the University of Pennsylvania and a Post-Doc at the Salk Institute for Biological Studies. He worked at at X-Ceptor Therapeutics, which was acquired by Exelixis in 2004, then in 2005 co-founded Syndax Pharmaceuticals, a NASDAQ-listed, clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies with three clinical stage assets.

Management team

Melanie Leydin, B Bus (Acc. Corp. Law)
Company Secretary

Melanie Leydin holds a Bachelor of Business majoring in Accounting and Corporate Law. She is a member of the Institute of Chartered Accountants and is a Registered Company Auditor. She graduated from Swinburne University in 1997, became a Chartered Accountant in 1999 and since February 2000 has been the principal of chartered accounting firm, Leydin Freyer.

Deanne Greenwood, BSc (Hons), PhD, MBA, GAICD
Vice President, Business Development & Intellectual Property

Dr Greenwood's efforts are focused on commericalisation of the Deoxymab assets and management of the extensive intellectual property portfolio. She has considerable experience related to research, drug development, relationship management, contracts and grants.

Valentina Dubljevic, BSc, MBB, GAICD
Vice President, Scientific & Clinical Development

Ms Dubljevic is responsible for the pre-clinical and clinical development of Patrys' products. Ms Dubljevic brings more than 20 years of scientific and commercial experience in the areas of anti-cancer therapies, vaccine development, and diagnostics.

Patrys snapshot

A noble goal

Here at Patrys we are deeply motivated to improve the lives of people diagnosed with aggressive forms of cancer, particularly cancers within the central nervous system which are often very difficult to reach and treat. We are in the pre-clinical stage of examining the potential of our technology, which is a noble journey underpinned by teamwork – with patients, researchers, clinicians and existing treatment providers too.

Novel technology

Patrys is innovating methodically and with great care, to uncover the full potential of its Deoxymab 3E10 platform. Patrys' rights to Deoxymab 3E10 are part of a worldwide license to develop and commercialise as anti-cancer and diagnostic agents a portfolio of novel anti-DNA antibodies and antibody fragments, variants and conjugates discovered at Yale University.

Deoxymab 3E10 is a DNA damage-repair (DDR) antibody that was first identified in lupus as an autoantibody that bound to normal cells. Of particular interest is that whilst most antibodies bind to cell surface markers, Deoxymab 3E10 penetrates into the cell nuclei and binds directly to DNA where it inhibits DNA repair processes and kills cells that have mutations or deficiencies in DNA repair mechanisms as found in various cancer cells.

Deoxymab 3E10 has single agent therapeutic potential and has been shown to significantly enhance the efficacy of both chemotherapies and radiotherapies. Deoxymab 3E10 can also be conjugated to nanoparticles to target delivery of chemotherapeutics and imaging agents to tumors.

A targeted solution for aggressive cancer

Patrys has developed a humanised form of Deoxymab 3E10, PAT-DX1 with improved activity over the original version of 3E10, and is progressing this, and a nanoparticle-conjugated form (PAT-DX1-NP) towards the clinic. In a range of pre-clinical studies PAT-DX1 has shown significant ability to kill cancer cells in cell models, human tumor explants, xenograft and orthotopic models. Treatment with PAT-DX1 has been shown to significantly improve survival in orthotopic models of both triple negative breast cancer brain metastases and glioblastoma. PAT-DX1 has also been shown to enhance the therapeutic effect of low dose radiation.

Patrys is targeting cancer at the nexus of two transformative anti-cancer therapies – antibodies and synthetic lethality. Antibodies target and kill cancer cells with fewer side effects than small molecules. While in synthetic lethality, DNA damage response (DDR) inhibition blocks 'back up' DDR systems, causing cancer cell death across a broad range of cancers – while healthy cells are spared.

Treatment with PAT-DX1 has been shown to significantly improve survival in orthotopic animal models of both triple negative breast cancer brain metastases and glioblastoma.

Single agent

Synthetically lethal (targets the DNA damage repair (DDR) process) as a single agent to block tumour cells' ability to repair

Combination therapy

Couple DDR with existing therapies, such as radiation, to create synergistic, anti-cancer effects

Antibody drug conjugates

Delivering highly potent cancer-killing agents or drugs directly to cancer cells via a linked nanoparticle

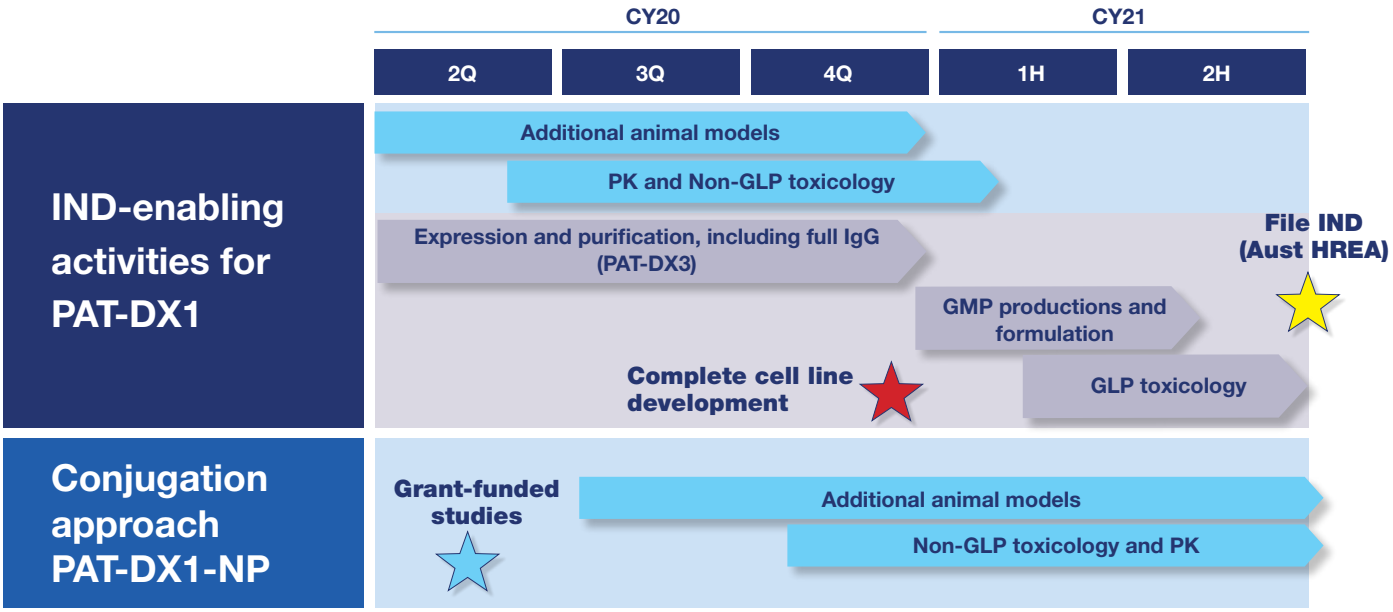
A promising future

Patrys believes that PAT-DX1 may have application across a wide range of malignancies such as gliomas, prostate, breast, pancreatic and ovarian cancers.

Preferentially localises to tumors	and is specifically attracted to extracellular DNA from dying cancer cells.
Penetrates the cell membrane and nucleus	PAT-DX1 is agnostic to tumor type or the presence of specific tumor markers.
Kills cancer cells deficient in DNA repair	PAT-DX1 diminishes cancer cells' ability to repair themselves. PAT-DX1 is able to target primary and secondary tumors and has a high therapeutic value against a wide range of cancer repair pathways such as those with mutations in the BRCA1/2 and PTEN genes.
Crosses the blood brain barrier	PAT-DX1 is able to resolve one of the greatest challenges in the development of therapeutics for brain diseases.

Pipeline

Patrys is working hard to give people diagnosed with cancer more targeted treatment options. Our initial focus is on Glioblastoma (GBM) and Triple Negative Breast Cancer (TNBC), with plans to expand into other solid tumors in future.



Commercial Milestones

During FY20 Patrys was pleased to announce a fully underwritten, non-renounceable Rights Issue to raise approximately A$4.29 million before costs. The proceeds raised will be applied to a series of value crystallising stages including; stable cell line development; toxicology studies and filing for a clinical trial in late 2021 and early 2022. Proceeds of the Rights Issue will also be used to support development of PAT-DX1-NP and other formats of the antibody, fund operations, the cost of the issue, working capital, and other business development and corporate activities.

Path ahead

Initiation of non-GLP toxicology and pharmacokinetic studies	Q3 2020
Expansion of Deoxymab platform applications (eg. nanoparticles)	Q3 2020
Completion of stable cell line development	Q4 2020
Initiation of GMP production and formulation program	Q1 2021
Initiation of GLP toxicology studies	H1 2021
IND (as Australian HREA) submission	H2 2021/H1 2022
Scientific publications	Ongoing
New IP filings and patent grants	Ongoing
Alliances and collaborations	Ongoing

Intellectual property

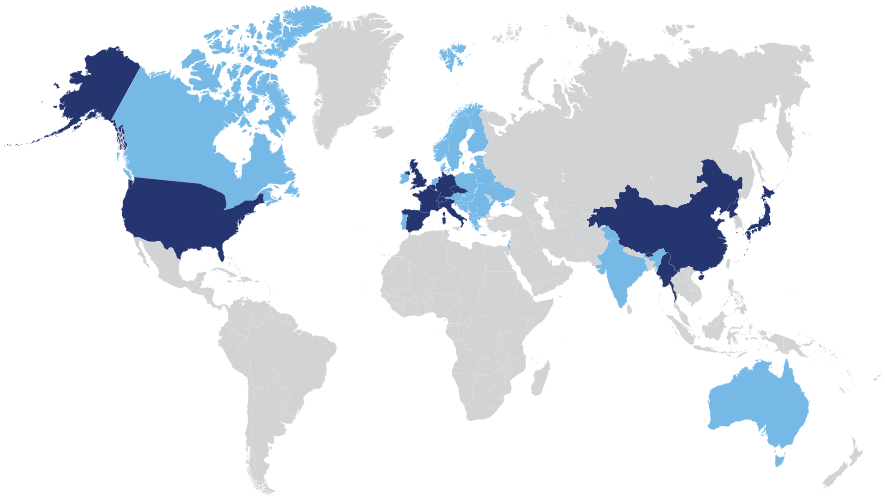
Patrys holds a central position in the cell penetrating antibody IP landscape with a wide portfolio of patents and patent applications covering both the composition of matter and application of Deoxymabs in multiple fields including cancer. The first patent in the 3E10 portfolio was granted in the US in July 2017 and further patents were granted in Japan and China in July 2018. The most recent patent in the Deoxymab portfolio was granted in Europe in July 2019 and covers methods of using Patrys' novel Deoxymab 3E10 technology, including Patrys' lead candidate (PAT-DX1), as treatment for a broad range of cancers and malignancies including gliomas, metastases, breast, pancreatic, ovarian and prostate cancers. Patrys continues to focus on maintaining patent protection in major jurisdictions where future regulatory approvals and product sales are targeted, with 19 pending patent applications across 10 patent families.

"Patrys remains focused on building and maintaining patent protection across key jurisdictions. Patrys has secured patent protection in some of the world's largest pharmaceutical markets including USA, Europe, China and Japan, Patrys is well positioned to preserve future product sales in key target markets."

- Patrys CEO and MD, Dr James Campbell

Active intellectual property strategy in place to protect key assets

Patrys' Deoxymab patent portfolio[1]



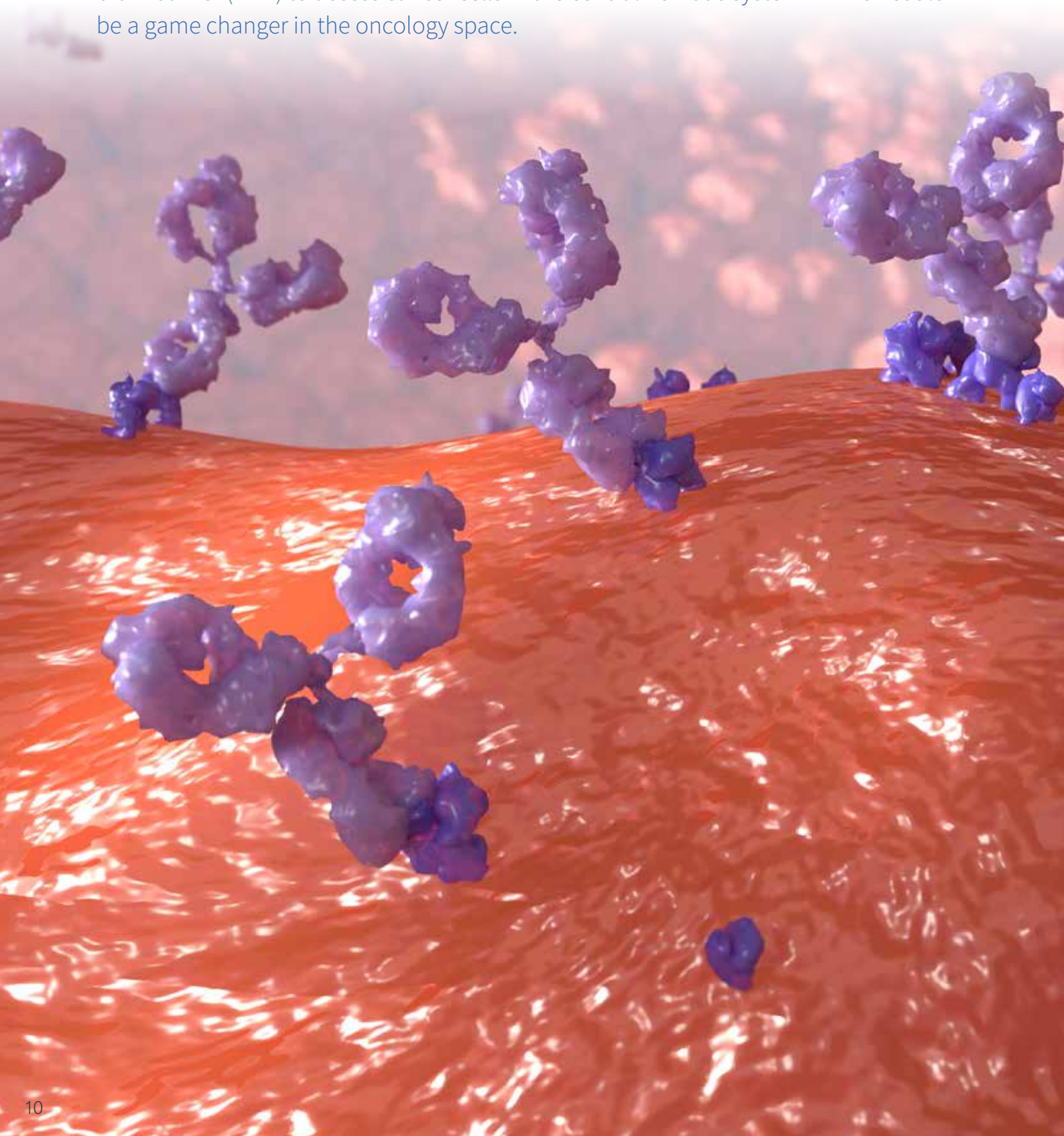
IP protection granted IP protection pending

Deoxymab patent portfolio

10	Active patent families
5	Granted patents[2]
19	Patent applications pending[1]

A closer look at Patrys' research

Exploiting synthetic lethality as a therapeutic approach means more people will survive cancer – that's our aim at Patrys. Our research shows that PAT-DX1 exploits the DNA Damage Response (DDR) mechanism to block DNA repair and preferentially kill cancer cells. Unlike other antibodies and 98% of small molecules, it can also cross the blood brain barrier (BBB) to access cancer cells in the central nervous system – which could be a game changer in the oncology space.



DDR therapeutics and synthetic lethality: a new frontier in cancer treatment

This year has marked promising progress for Patrys' lead asset, PAT-DX1, highlighting its capabilities to exploit the DNA Damage Response (DDR) mechanism to block DNA repair and preferentially kill cancer cells.

In simple terms, PAT-DX1 blocks DNA repair and, as demonstrated in animal models, it kills cancer cells with a range of DDR gene mutations such as BRCA2 and PTEN. Importantly, it does not kill cells without those mutations.

PAT-DX1 is unique because it is the only antibody to have shown innate efficacy as a single agent via the synthetic lethality model. PAT-DX1, unlike other antibodies and 98% of small molecules, is also able to cross the blood brain barrier – the all-important ticket to killing cancer cells in the central nervous system.

Here's a closer look at the science of DDR for context.

In a healthy person many thousands of events of DNA damage occur every day, like radiation exposure from sunlight or exposure to toxins. As DNA damage impairs the ability of the body to function normally, our bodies have an elegant system of repair mechanisms to identify and fix DNA damage.

The DDR mechanism consists of more than 450 proteins that work to identify and rectify damage to the genome. There are several different types of DNA damage, ranging from small breaks in one strand of the DNA helix through to double strand breaks and even replication errors. The five different classes of DNA damage have resulted in the evolution of five major DDR pathways.

As cancer cells emerge, they develop changes in a variety of cell functions that result in abnormal cell growth and potential to spread to other parts of the body. As part of the transformation, most cancer cells lose some of their DDR machinery and the ability to repair DNA damage in at least one of the five major pathways.

Even though cells are optimised to use specific DDR pathways, there is a degree of redundancy involved, meaning that a cancer cell with a fault in one DDR pathway will use the other pathways to try to fix arising DNA damage. With the ability to use less than perfect tools to patch up DNA damage, cancer cells can continue to thrive and proliferate.

This is when things get really interesting. Researchers asked what would happen if they were able to block the back-up DDR system from working – could it kill the cancer cells?

The logic was that if one DDR pathway is not working because of a biological reason (the genes for the pathway were turned off during the process of becoming a cancer cell), blocking an additional pathway by therapeutic means should deactivate the whole DDR system in the cancer cells and lead to cancer cell death.

This therapeutic approach is known as synthetic lethality and has the advantage that it is the combination of two DDR pathways not working that is lethal, and that normal cells with intact DDR systems should not be killed by the DDR therapeutic. It remains a focus area for many players in big pharma and indeed, a significant point of value in the R&D portfolio of our growing company.

"PAT-DX1 is unique because it is the only antibody to have shown innate efficacy as a single agent via the synthetic lethality model."

- Patrys CEO and MD, Dr James Campbell

Blood brain barrier

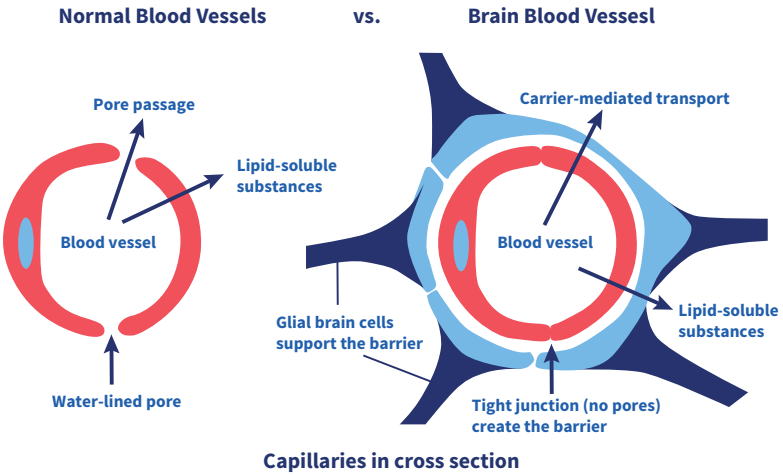
Crossing the blood brain barrier (BBB) is a pivotal function for new therapeutics in the treatment of brain cancers – and one of the key reasons why Patrys' PAT-DX1 asset, and more broadly the Deoxymab platform, is so promising.

The common understanding of the BBB is that it is a barrier that surrounds the brain, and plays two major roles; stopping infectious agents like bacteria and viruses from entering; and insulating the brain from rapid changes in the concentrations of nutrients and other compounds. It is convenient to think of the BBB as a shield, protecting and controlling, and there is a lot of imaging that reinforces this understanding, like the picture at right. This understanding helps people to visualise what is happening when they hear, for instance, 'Almost no large molecules and 98% of all small molecules do not cross the BBB'.

The truth is a bit more complicated than this broad-brush understanding. The BBB is not an impenetrable protective sphere that surrounds the brain, but is rather a refinement of blood vessels, and specifically the smallest blood vessels called capillaries, that tightly control what can enter this most critical and sensitive of organs. If joined end to end, these brain capillaries would be 650 km long.

To understand what makes the BBB so special, we need to understand the difference between highly specialised capillaries in the brain and capillaries that flow through all other organs in the body. Capillaries feed tissues with required nutrients and gases, and help remove waste products. These interchanges of nutrients, gases and wastes are feasible because in most instances the capillaries are not "closed" systems. There are gaps between the cells that make up capillaries' walls in a majority of tissues – these gaps are not so big that blood cells can leave the capillaries, but many other substances such as nutrients, proteins, antibodies, drugs and even pathogens can freely transverse capillaries' walls.

In contrast the cells of capillaries in the brain are joined by tight junctions, meaning there are no gaps between cells, but rather a range of very specific transporter channels that selectively allow the exit or entry of a very small number of essential nutrients, wastes, and peptides. The outside of the capillary is reinforced by specialised neural cells called glial cells that strengthen and support the vessel.



1 Wong, A. D. *et al.* (2013). The blood-brain barrier: an engineering perspective. Front Neuroeng 6:7.

Whilst the capillaries in the body create an open system that allows most molecules, proteins, drugs and even pathogens free access, the capillaries in the brain act like sentinels, and only allow entry of few vital molecules – but prevent entry of circulating toxins and pathogens that could cause brain infection.

Therein lies the downside and challenge as the vast majority of potential drug treatments are not allowed entry across BBB either.

Delivery of therapeutics, either small molecules or biologics/antibodies to cancers outside of the brain is enabled by the leaky capillaries, but delivery of therapeutics to cancers within the brain is very difficult, because the gatekeeping transporters need to be tricked into allowing these foreign substances across the threshold of the brain. That's why there is so much interest in the development of new drugs and/or technologies to enable transit of the BBB.

Our collaborators at Yale School of Medicine have previously shown that the Equilibrative Nucleoside Transporter number 2 (ENT2) controls the entry of PAT-DX1 into cancer cells before it stops DNA repair and causes cancer cell death. We also know that ENT2 is highly expressed in the capillaries of the brain.

This means that PAT-DX1 has the keys to open the BBB, and as we've previously reported, has shown an ability to reduce the growth of both primary cancers like glioblastoma as well as metastases in the brain.

That's why we think that PAT-DX1 is so very interesting.

Research platform expansion

Designing complex antibodies

Our immune system acts like a security checkpoint. This high-tech system inside the human body identifies and mobilises what kind of antibodies we need to protect us from foreign invaders.

Antibodies are typically Y-shaped proteins which are produced by the immune system to neutralise pathogens such as bacteria and viruses. A classical antibody's two arms will bind specifically to one binding site. The modular architecture of antibodies means this traditional shape can be exploited to make different antibody formats.

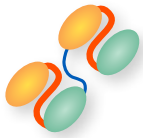
Patrys' Deoxymab platform consists of the murine 3E10 antibody which has now been optimised and humanised. The reformatted antibody has been re-named PAT-DX1. Instead of making a traditional antibody the Patrys team has designed a new format of PAT-DX1, a smaller di-single chain fragment antibody as our lead candidate. Our researchers believe that a smaller protein may have improved penetration capabilities leading to better killing of cancer cells.

We have utilised this format of PAT-DX1 for a number of pre-clinical studies where we have, for example, seen increased tumour suppression in brain cancers and metastases and the ability of PAT-DX1 to cross the blood brain barrier.

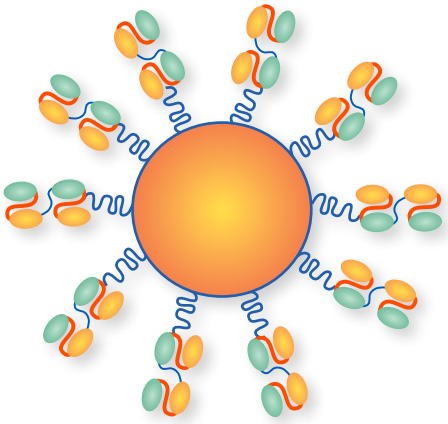
Patrys' team also recognises that the traditional Y-shaped antibody features maybe important in certain clinical settings and will investigate a full IgG antibody based on Deoxymab 3E10. It is envisioned that a range of formats of Deoxymab antibodies will provide a great opportunity to tailor the design of the antibody to match the intended clinical application.

As our understanding of biology around the unique Deoxymab platform increases, we continue to gain a better understanding of what features will make a therapeutic antibody more effective.

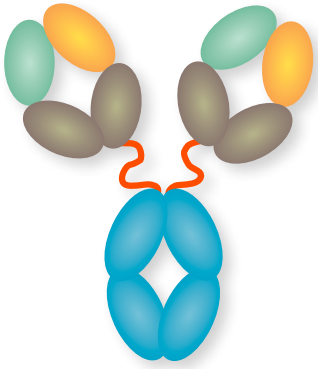
PAT-DX1



PAT-DX1-NP



PAT-DX3



Collaborations

Patrys is fortunate to be working with a number of academic collaborators and institutes both in Australia and the US. Our research partners in the US have attracted grants worth more than $A4.87 M from the National Institutes of Health (NIH) and the Department of Defense (DoD) in United States this financial year. Patrys' latest research collaboration in Australia is with the Olivia Newton-John Cancer Research Institute (ONJCRI), which has been awarded a $50,000 Federal Government grant to support research at ONJCRI on Patrys' PAT-DX1 program. The aim of this program is to determine the efficacy of PAT-DX1 in *in vivo* studies of breast cancer with DNA damage repair (DDR) defects. The effect of PAT-DX1 on regression of primary and metastatic breast cancers will be assessed in combination with standard-of-care radio and chemo-therapies. Looking forward, Patrys and the ONJCRI plan to expand this collaboration to include both PAT-DX1 conjugated to nanoparticles (PAT-DX1-NP) and anticipated new formats of the Deoxymab platform. We look forward to reporting on the research finding from these grants from 2021 onwards.

Corporate directory

DIRECTORS	Mr. John Read (Non-Executive Chairman) Dr. James Campbell (Managing Director & CEO) Mr. Michael Stork (Non-Executive Director and Deputy Chairman) Ms. Suzy Jones (Non-Executive Director) Dr. Pamela Klein (Non-Executive Director)
COMPANY SECRETARY	Ms. Melanie Leydin
REGISTERED OFFICE	Level 4, 100 Albert Road South Melbourne VIC 3205 Phone: 03 9692 7222
PRINCIPAL PLACE OF BUSINESS	Level 4, 100 Albert Road South Melbourne VIC 3205 Phone: 03 9692 7222
SHARE REGISTER	Computershare Investor Services Pty Limited 452 Johnston Street Abbotsford VIC 3067 Phone: 1300 850 505 (within Australia) Phone: +61 3 9415 5000
AUDITOR	BDO Audit Pty Ltd Tower 4, Level 18, 727 Collins Street Melbourne VIC 3008 Australia
STOCK EXCHANGE LISTING	Patrys Limited shares are listed on the Australian Securities Exchange (ASX code: PAB and Listed Options: PABO)
WEBSITE	www.patrys.com
ANNUAL GENERAL MEETING	Patrys Limited advises that its Annual General Meeting will be held on Thursday, 19 November 2020. The time and other details relating to the meeting will be advised in the Notice of Meeting to be sent to all shareholders and released to ASX in due course. In accordance with the ASX Listing Rules and the Company's Constitution, the closing date for receipt of nominations for the position of Director are required to be lodged at the registered office of the Company by 5.00pm (AEST) on 1 October 2020.

Corporate and social responsibility

Patrys is a leading therapeutic development company developing a platform of cell-penetrating antibodies for a range of cancers. In pursuing this objective, Patrys acknowledges its role within society and believes its success will deliver long-term positive benefits to all stakeholders. Patrys' corporate governance principles and code of conduct set the framework for how the company, management and employees are expected to conduct themselves.

Our people

The employees of Patrys are essential to the company achieving business success. To ensure Patrys remains a safe, healthy, and attractive workplace for our employees, Patrys has established workplace policies and practices.

Patrys' code of conduct reflects the core values of the company and sets out standards of behaviour in matters including compliance with all legal operations of the company. Patrys has significantly lower rates of employee turnover than the industry average. This higher rate of employee retention is indicative of its positive and collegiate workplace. Patrys prides itself on a strong culture based on accountability, performance, and ethical and respectful behaviours. The Board has adopted a diversity policy to provide a framework for Patrys to achieve a number of diversity objectives including, but not limited to, gender, age, ethnicity, disability, sexual orientation and cultural background. Within the limits of a small organisation, Patrys believes that it is tracking well on measures of diversity, including five of the eight leadership roles in the Board and Management being held by females, and similarly five being born outside of Australia. Patrys strives to put in place measures, such as flexible working arrangements, specifically to encourage participation by all.

Employee option schemes are used to provide the opportunity for all staff to share in the success of the company and to assist in aligning the objectives of employees with those of shareholders.

The community

Through innovative research and development, Patrys is creating products for needs which are currently unmet within the health and medical markets. All of Patrys' preclinical research activities comply with strict regulatory and ethical approval processes.

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