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Shareholder Newsletter

MARCH 2023

What's inside

Hello from our CEO and MD, Dr James Campbell

This is a defining calendar year for Patrys (ASX:PAB) as we work methodically towards our goal of commencing a first in-human clinical trial of PAT-DX1.

We are on the cusp of learning about the therapeutic capabilities of this novel antibody. Specifically, its utility for treating brain and non-brain cancers with existing DNA damage response (DDR) deficiencies and its activity in combination with other DNA damaging agents such as radiation and chemotherapy drugs. We are optimistic and prepared.

Preparation is key and we wholeheartedly respect the process of planning and successfully executing this clinical trial. French chemist and microbiologist, Louis Pasteur, famously declared in 1854 “chance favours the prepared mind”, and nothing could be more true at this stage of our development. By the end of 2023, our plans are to have completed the ongoing toxicology studies for PAT-DX1; to have received clinical approval for our planned phase 1 study; to have completed manufacturing of the clinical batch of PAT-DX1 material; and to have initiated our long-awaited clinical trial.

Our team is experienced and expanding to take PAT-DX1 to the clinic. Last year we welcomed Dr Rebecca Tunstall as Vice President Corporate Development, and Dr Charmaine Gittleson as Chairman. Within this newsletter, you can read about Charmaine’s experience in the life sciences space, together with her focused motivations for embracing this leadership role.

In addition to our primary clinical program, we are investing time and resources into **business development activities** including directed research activities and **ongoing engagement with our research partners** – including the Telethon Kids Institute, the Olivia Newton-John Cancer Research Institute, the Garvan Institute of Medical Research and Monash University. We acknowledge the support of various funders including the Cure Brain Cancer Foundation and the Victorian Medical Research Acceleration Fund, and look forward to sharing research updates in 2023.

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Hello from our CEO and MD, Dr James Campbell *(continued)*

We are also committed to advancing the development of our second deoxymab, PAT-DX3, and expanding our understanding of its clinical potential. We are in the process of finalising a master cell bank (MCB) for the production of PAT-DX3, and are well advanced with preliminary process development work. I look forward to sharing outcomes of our investigations as they unfold.

At Patrys, we believe our work has the capacity to change the landscape for hard to reach and treat cancers. We know that numerous cancers don't have suitable cell surface markers, so are resistant to traditional antibody approaches. We also know that no anti-cancer therapeutic antibodies have been able to cross the BBB, meaning that antibodies have not been widely used for the treatment of brain cancers. **Our deoxymab platform is designed to overcome these hurdles and if successful, will be truly revolutionary.**

On behalf of the extended Patrys team, I would like to **thank our supporters and investors** who are backing us during this critical chapter. We have a clear plan and remain energised about what we will experience and learn about our technology along the way – innovation truly is the best adventure.

With you in health and business,

Dr James Campbell

Home ground advantage: Why Patrys is keeping things local

According to a 2021 report by MTP Connect, titled *"Australia's Clinical Trials Sector: Advancing innovative healthcare and powering economic growth"*, clinical trials are a booming industry in Australia. Approximately 1,880 clinical trials were conducted in Australia in 2019, recruiting approximately 95,000 participants and representing approximately $1.4 billion in expenditure across the sector.

Planning and conducting a trial in Australia offers a lot of advantages for a company like Patrys. A thriving medical research community, a reputation for producing quality data that is highly regarded by international regulators, and strong clinical trials infrastructure on our doorstep are just some of the reasons why it makes sense for Patrys to run its upcoming Phase 1 clinical trial of PAT-DX1 in Australia. Not to mention the economic benefits via tax offsets for eligible R&D activities carried out in Australia.

Under the Australian government's Research and Development Tax Incentive (R&DTI), eligible companies can receive a tax offset for eligible R&D activities. The scheme is designed to encourage investment in R&D, helping companies to grow and contribute to the Australian economy. Earlier this year, Patrys announced a $3.35 million R&D Tax Incentive Refund for the 2021/22 financial year - an outcome that Patrys CEO James Campbell said would support the Company "to confidently continue advancing PAT-DX1 towards the clinic in the second half of 2023".

Equally important are practical considerations. In a global context, ethics and regulatory processes are considered a rate-limiting step to the commencement of a clinical trial, but Australia boasts one of the most streamlined and efficient regulatory environments in the world, which contributes to efficient start-up timelines. Working with local vendors can also mean better collaboration, greater oversight, and ultimately more control over how the trial is managed.

According to Patrys' Vice President Corporate Development, Dr Rebecca Tunstall, these are all practical considerations for the Company, as it plans its first in-human trial of PAT-DX1 for later this year.

"We're currently talking to Contract Research Organisations (CROs) to run the clinical trial."

"Working with an experienced local CRO will mean that we're in a better position to understand how they work, who's in their team, leverage their strengths and expertise, and build a successful partnership. In addition, having the team here in Australia makes it far more practical in terms of managing communications - we're not having to manage time-zone differences, which simplifies communication and creates efficiencies."

Australia is increasingly becoming a competitive environment for Phase 1 oncology trials, so how does a company like Patrys secure the interest of clinical investigators?

Early engagement is key, Rebecca says:

"We've been talking to potential investigators for the trial, explaining the mechanism of action for PAT-DX1, and talking through the pre-clinical safety and efficacy data to date. Our goal is to get on their radar early, and engage with them about the potential of our technology for their patients."

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Home ground advantage: Why Patrys is keeping things local

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Feedback from clinicians is also helping to inform the trial design. Understanding the current standard of care, and how a patient is routinely progressed through treatment is a vital part of the planning process.

"We need to ensure that the trial is attractive to both the patients and the clinical investigators, so that when we come to recruiting participants into the trial, we're not presenting barriers for them to become involved."

"As the critical elements come together, and the Company moves towards trial initiation, it's obvious that running a clinical trial in Australia offers Patrys a home ground advantage, which will serve us well into the clinic, and beyond."

Reasons why Australia is a leader in clinical trials

- Globally recognised community of medical experts and research
- International reputation for producing high quality research and data, and compliance with Good Clinical Practice Guidelines (GCP) that are looked upon favourably by regulators
- Dedicated clinical trials infrastructure, and investment by government to maintain and strengthen this infrastructure
- Streamlined regulatory and ethics approvals processes
- Tax relief provided by the Research and Development Tax Incentive enhances Australia's cost competitiveness as a destination for clinical trials.

Source: "Australia's Clinical Trials Sector: Advancing innovative healthcare and powering economic growth", MTPConnect, 2021

Advancing deoxymabs to the clinic

Prior to dosing patients in the clinic, there is a significant body of work to be completed in the background to ensure that a new therapy is both safe and effective for in-human trials, and that the necessary data package is generated to meet regulatory requirements.

Making antibodies on a commercial scale can be a complicated and multi-faceted process. Patrys' Vice President, Research and Development, Valentina Dubljevic, oversees the pre-clinical and manufacturing development of Patrys' deoxymabs, a role which is keeping her busy as milestones are met in the lead up to the Phase 1 clinical trial.

"There are numerous pre-clinical activities running concurrently at the moment - including manufacturing, pharmacology and toxicology studies - all of which are integral to the clinical trial design, and will inform the trial protocol," Valentina explained.

"A planned, and coordinated approach is crucial at this point to ensure that the sequencing of activities is right, and that we have all the necessary documentation to support our ethics application for the trial."

Leading this specialised body of work is a high-performing cross functional team, as well as established relationships with key collaborators and stakeholders.

"We are very fortunate to have long standing relationships with a number of highly reputable and reliable collaborators and external consultants, who are well respected in our industry. We liaise extensively with these experts on all aspects of planning - whether it's manufacturing, or toxicology or the clinical trial itself, we engage with technical advisors who oversee the process and make sure that we're on track."

In parallel is the ongoing development of Patrys' full-size antibody, PAT-DX3, and exploring its potential in a range of indications and applications.

"The work we are doing at the moment has many moving parts. We're not just looking at the immediate needs of the PAT-DX1 trial, but at a more macro level, we're also considering the work Patrys may undertake into the future. Therefore, from a risk management perspective, it is crucial for us as a Company to partner with people we trust, and who are invested in helping us to achieve our objectives with the utmost scientific rigour."

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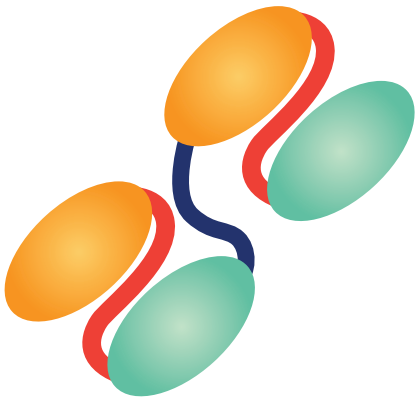
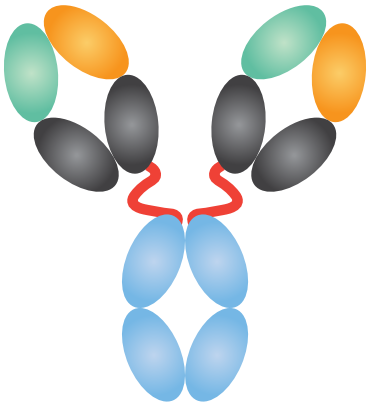


PAT-DX1 antibody fragment



PAT-DX3 full sized antibody

Advancing deoxymabs to the clinic

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What's happening right now?

Manufacturing

The Patrys team has been working in close partnership with its Contract Development Manufacturing Organisation (CDMO) to refine the manufacturing process to meet Good Manufacturing Practice (GMP), and ensure that the production process for deoxymab, PAT-DX1, is both robust and consistent.

Patrys is currently preparing for a GMP run of PAT-DX1, to produce the high-quality clinical material required for the Phase 1 clinical trial. In mid-2022, the Company announced the successful completion of an engineering run of clinical-grade PAT-DX1. The resulting antibody product met all the specification requirements for GMP, and the same process will be applied to the upcoming GMP run.

Toxicology and Pharmacology studies

The objective of toxicology and pharmacology studies is to determine a safe and effective PAT-DX1 starting dose for a first-in-human trial.

Toxicology studies are required to determine the safety of a new therapy when administered to a patient. In first in-human trials, this is especially important in order to ensure that the therapy poses no harmful risk to the patient.

GLP toxicology studies of PAT-DX1 in two species (rats and non-human primates) are currently underway. These studies will assess PAT-DX1's safety profile and determine its toxicity and potential side effects.

The results of these toxicology studies will help to establish the safe starting dose for the clinical trial, and identify any potential adverse effects that may occur.

However, in a population of patients with serious conditions, such as cancer, the team must not only consider which dose of PAT-DX1 is safe, but rather *what is the appropriate dose range for the study that will be safe but likely to elicit some therapeutic response as well.*

Pharmacology studies are investigating how PAT-DX1 works and interacts with the body and will help determine the minimum anticipated biological effect level (MABEL) to guide selection of the first human dose . Patrys is currently conducting studies in animal models of cancer to determine starting dose for the trial as well as dose range and schedule that is both safe and likely to result in clinical efficacy.

Good Manufacturing Practice (GMP) is a set of guidelines and procedures that ensure the quality of therapeutic goods. In the pharmaceutical industry, GMP plays a crucial role in ensuring that new therapies meet regulatory standards for medicinal products. These guidelines cover every aspect of the manufacturing process, including facility and equipment standards, hygiene practices, materials management, documentation and record-keeping, packaging and labelling, and storage and distribution of materials. By adhering to these strict standards, manufacturers can ensure that their products are safe, effective, and of high quality for human use.

DDR landscape: How the numbers stack up

A closer look at DNA Damage Response (DDR)

Cancer often develops or starts to spread because of changes (mutations) that can accumulate at a high frequency in the DNA inside cancer cells. These mutations often lead to changes in the expression of the genes that normally control the growth and proliferation cells in the body. These mutations can also activate genes that allow cancer cells to migrate to other sites in the body—a process called metastasis.

Because changes in DNA can have such a major impact, the body has developed a number of systems that are dedicated to preventing, detecting and repairing damage to DNA. These systems—which are collectively known as DNA damage response (DDR) systems—are designed to prevent cells with faulty DNA from reproducing by either repairing the damage before the cell divides, or by triggering the cells with damaged DNA to effectively commit suicide.

Patrys is exploiting this natural system for eliminating cells with damaged DNA as an approach for treating patients with cancer. Patrys' deoxymabs are able to enter the cell and cell nucleus where they can bind to DNA and prevent its repair. As cancer cells often have a large number of mutations that need to be repaired, blocking these repair systems can effectively put them on a pathway where they will die if they try to divide.

There are a number of proteins in the cell that are involved in the DNA damage response—including special enzymes called nucleases, helicases, and polymerases—and these provide potential targets for drugs. One class of drugs that has successfully used this approach for treating cancer is the PARP inhibitors (PARPi). In certain cancers where the DNA damage response system is already compromised and not working fully, such as breast cancers with the BRCA mutation, the addition of a PARP inhibitor can "tip them over the edge" and result in the accumulation of sufficient DNA damage that the cancer cells start to die. Adding a PARP inhibitor to a cancer cell which already has a compromised DDR is an approach called "synthetic lethality", or SL. Since the publication of the PARP/BRCA synthetic lethality (SL) pairing in *Nature* in the early 2000's, the DDR approach has attracted a lot of interest, and several developers are now trying to use a precision medicine approach via targeted therapies.

The first PARP-targeted clinical trial of the PARP inhibitor Rucaparib was in 2003, and the DDR landscape has now expanded to include over 100 clinically active assets, across a breadth of targets.
(Source: Beacon Data, 2022)

DRR in the clinic – the rise of a second generation?

- Until recently, the only DDR-relevant drugs to be approved for the treatment of breast cancer were PARP inhibitors such as Niraparib. This class of drugs has been successful because breast cancers often harbour a BRCA mutation/deficiency which hamstrings the cell's DDR systems and results in synthetic lethality when combined with PARP inhibition.
- There are currently four FDA-approved PARPi that belong to the first generation of DDR therapies acting on PARP1, PARP2, and in the case of Rucaparib, PARP3.
- A second generation of PARP1-selective, and non-PARP targeted assets are starting to gain momentum and were the focus of significant clinical activities in 2022. Patrys' PAT-DX1 and PAT-DX3 belong to this non-PARP class of drugs targeting DDR.

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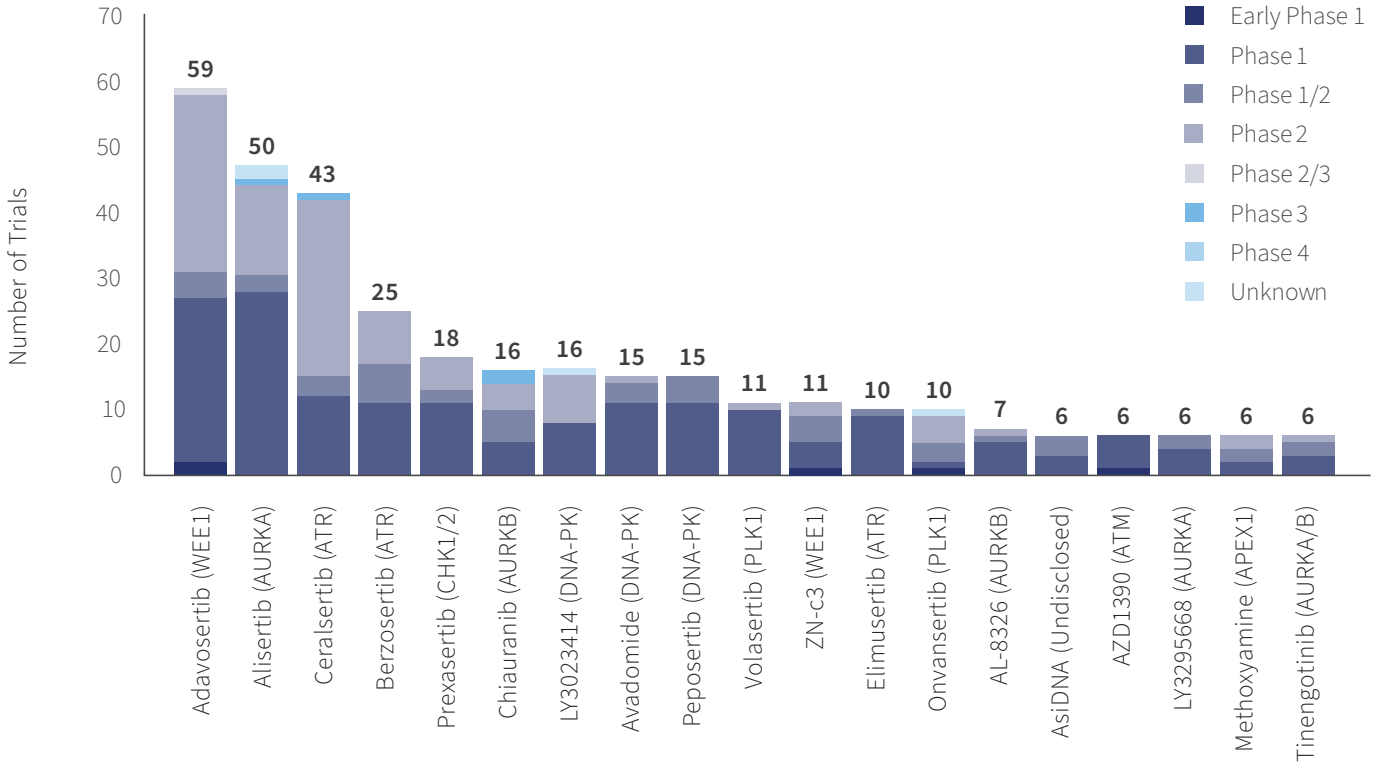
DDR landscape: How the numbers stack up *(continued)*

DDR trials initiated since 2011

(Data accurate as of 3 February 2023. Source: Beacon by Hanson Wade.)



The DDR targeting therapeutics market is projected to be worth USD $1.0 billion in 2030, growing at an annualised rate of 52.6% during the period 2024-2030.

> “Patrys’ antibodies target the DNA fragments that are released from dying cancer cells, meaning they work independently of cell surface markers of cancer. They localise to the tumour environment very quickly – in a matter of minutes – and are internalised into the cell nucleus where they block DNA repair and DNA replication, leading to cancer cell death.”
>
> **- Patrys CEO and MD, Dr James Campbell**

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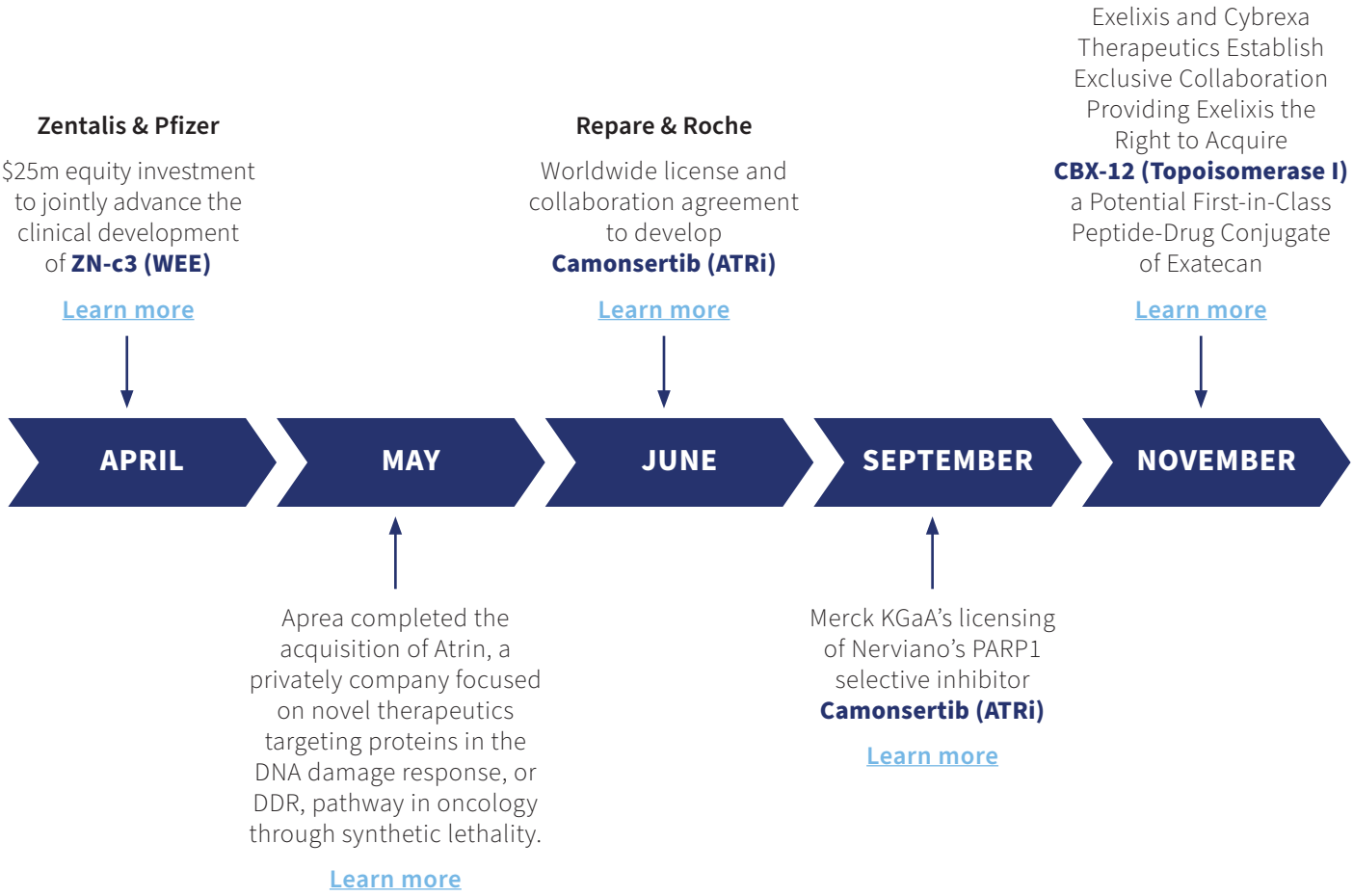
DDR landscape: How the numbers stack up *(continued)*

DDR Market Deals



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DDR landscape: How the numbers stack up *(continued)*

Triple Negative Breast Cancer (TNBC)

- Treatment guidelines for treating breast cancer patients that have a mutation in their HER2 gene (TNBC patients) are well established globally. TNBC is still sensitive to some chemotherapy drugs and so this treatment remains the standard of care despite its limited effectiveness.
- Recent advances with novel agents have been made for specific subgroups of patient such as those with PD-L1+ tumours or germline BRCA-mutated tumours. However, only a fraction of these patients respond to immune checkpoint or PARP inhibitors and those who do respond still often develop resistance and relapse.
- As a rule, patients with advanced breast cancer featuring low HER2 expression levels are diagnosed with HER2-negative disease because HER2-targeted therapies typically prove to be ineffective in this setting. In 2022, the FDA approved trastuzumab deruxtecan (Enhertu) for the treatment of HER2-low breast cancers that can't be removed surgically, or that have spread (metastasised) elsewhere. This approval is likely to change the treatment landscape for HER- BC and create opportunities for novel first in class drugs like deoxymabs that have the ability to address patient subgroups in breast cancer.
- AstraZeneca's **Olaparib** is approved in Japan as an adjuvant treatment for HER- patients. Lilly's **Abemaciclib** was approved for both HER2+ and HER2- with unresectable or recurrent breast cancer patients in Japan. These molecules are already marketed for HER2- BC in other geographies.
- Drugs that are approved in this space include Lynparza (olaparib) an antineoplastic agent. Olaparib is used to treat HER2- BC, ovarian cancer, pancreatic cancer, prostate cancer, fallopian tube cancer, and peritoneal cancer. It is currently under development for various oncological indications. **Global sales for Lynparza are expected to increase from over $2.4 billion in 2021 to approximately $6.4 billion by 2028.**
- The overall **TNBC market was valued at US$650 million in 2021**, and it is expected to grow with a CAGR of 4.4% during a forecast period of 2022-2030.

Glioblastoma

- There is a high level of unmet need in glioblastoma (GBM—a primary cancer of brain tissue) as patients have few other treatment options.
- The last breakthrough in the GBM space occurred in 2005, with improvement of survival of 2 months using a new chemotherapy drug temozolomide.
- Temozolomide (TMZ) is used to treat specific types of brain cancer in patients whose tumours have returned or whose tumours have just been diagnosed.
- TMZ has become a cornerstone of GBM treatment and is used in combination with radiotherapy. Unfortunately, due to the widespread exposure to TMZ and highly heterogeneous and mutation prone nature of GBM, it is quite common for these lethal tumours to develop resistance to TMZ.
- Although still in its early stages, Merck & Co. is now shifting attention to the use of immunotherapy and particularly Keytruda in combination with DNATrix's DNX-2401 for efficacy in GBM patients.
- There are at least 19 therapies in Phase III trials for GBM with some expected to launch in the 8 major markets in the next 3 years *(Source: Globaldata 2023.)*
- **GBM market sales reached $550 million in 2020 and are expected to increase to $850 million by 2030.**

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Q&A with Patrys Chairman, Dr Charmaine Gittleson

Dr Charmaine Gittleson was appointed as Patrys' Chairman of the Board of Directors in November 2022. She has an impressive track record in pharmaceutical development, both in Australia and the USA. She is the former Chief Medical Officer of CSL Limited, and her expertise spans many aspects of the pharmaceutical industry, from drug development and clinical research through to strategic planning and executive management. Charmaine also brings extensive regulatory experience to the Board, having successfully worked with regulators in key markets such as the US, EU, Asia Pacific, Japan and South America. Charmaine also has Board and Chairman experience, notably of the ASX-listed company Antisense Therapeutics.

In this short Q&A, she shares insight into what has motivated her to join the Patrys team.

Patrys Chairman, Dr Charmaine Gittleson

"I have been following the development of the Patrys platform for several years and continue to be very excited by the potential of deoxymabs to provide new approaches for treating a range of different cancers."

- Dr Charmaine Gittleson

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Q&A with Patrys Chairman, Dr Charmaine Gittleson *(continued)*

Q. Can you name an achievement, or series of achievements, that you've been proud to contribute to as a leader in Australia's biotech sector?

I established the CSL clinical trial pharmacovigilance and clinical strategy groups supporting global clinical trials – this involved developing local skills to lead related interactions with global regulatory agencies which was new for CSL at the time as well as the local biotech industry.

I led the clinical strategy team that developed an H1N1 influenza vaccine for the 2009 influenza pandemic facilitating release of the H1N1 specific vaccine in time for the Australian flu season. Our team were also the first in the world to publish clinical trial data on this pandemic vaccine (published in the NEJM).

I also established early development / First in Human (FIH) capability in Melbourne - again development of local skills to support transition of research compounds into the clinic.

Q. What has been your experience / exposure to First in Human (FIH) research in Australia and internationally?

I was instrumental in driving CSL's strategy in establishing a FIH clinical development capability, based in Australia. The group successfully designed and conducted FIH studies on novel compounds which have since moved into later clinical development.

I have overseen the global clinical development of a number of rare disease medications with successful approvals under multiple regulatory jurisdictions such as FDA, EMA, MHRA, PMDA and TGA.

I have also been privileged to be involved in many due diligence exercises and provided input on suitability for development.

Q. In your opinion, why is Patrys' area of research so compelling?

This is novel science, which in itself is exciting, but it is compelling because the proposed (or intended) mechanism of action will address an unmet need in cancer therapy. Being involved in development that could make a difference to people's lives is thrilling and what gets me up every day.

Q. From a commercial perspective, why does Patrys' research pipeline present such a valuable opportunity for investors?

The approach is novel, so a clinical candidate has the potential to be a first in class drug. The market is not limited to one cancer type thus affording lifecycle opportunities. The antibody works on a pathway present in all malignancies and is not cancer receptor dependent. This introduces potential optionality in terms of its applicability to various cancer types.

Additionally, the approach targets malignant cells which may translate to lower side effects and better patient tolerability, which in a commercial sense is reflected in strong uptake and compliance.