patrys

Shareholder Newsletter

July 2020

What's inside

01

Hello from our CEO and MD, Dr James Campbell

This has been a challenging quarter for businesses all around the world due to measures introduced to limit the spread of COVID-19 – so may I start by sharing best wishes to the people and companies who have experienced hardship and heartbreak during this time.

Here at Patrys we have made adjustments to our clinical development timelines and operational practices; but I am heartened by the work ethic and progress of our extended team and partners. We are moving steadily towards important pre-clinical milestones and have made promising business development progress too.

Highlights within this newsletter include a closer look at why synthetic lethality is attracting attention globally in some of the most influential oncology research circles. Relevant to our work at Patrys, PAT-DX1 blocks DNA repair and, in animal models with impaired DNA repair machinery, leads to selective killing of cancer cells.

As we all know, drug development is an exacting, time consuming and costly process. The team at Patrys has made significant advances with the PAT-DX1 program since it was in-licensed just four years ago, and is targeting a clinical trial at the end of 2021 or early in 2022. We have been delighted with two aspects of financing over the past few months, grant success for our collaborators and the launch of a fully-underwritten $4.3M Rights Offer, which is ongoing. The prospectus for the fully-underwritten Rights Offer announced by the Company on 22 June 2020 can be obtained at www.patrys.com. Offers to Eligible Shareholders have been made electronically in the personalised entitlement and acceptance form that accompanies the Prospectus. Eligible Shareholders should consider the Prospectus in deciding whether to acquire the securities. Eligible Shareholders who want to acquire the securities will need to complete the entitlement and acceptance form that accompanies the Prospectus prior to 5:00 pm AEST on 29 July 2020. This Rights Offer, which will raise $4.3M before costs, will fund a range of critical development activities on our path to the clinic, and will also be applied to broaden the development of the Deoxymab platform technology and working capital. In the near term this will mean exploring additional antibody formats and progressing a program of nanoparticle conjugation for targeted delivery of payloads across the blood brain barrier.

Later in this newsletter we also examine recent studies to establish the mechanism by which PAT-DX1 crosses the blood brain barrier (BBB) – revealing the coveted how of Patrys' platform technology.

We are motivated by a great sense of pride and purpose at Patrys to deliver a significant breakthrough in the oncology space. I look forward to honouring your contribution to, and support of, our Company by continuing our work to develop new, potentially life-saving, cancer treatments.

As a valued shareholder – and partner – in our business, I personally thank you for your ongoing support.

With you in health and business,

James Campbell

patrys

Refining the science of selective cell death

Patrys' lead asset PAT-DX1 exploits the DNA Damage Response (DDR) mechanism to block DNA repair and preferentially kill cancer cells. In animal models, PAT-DX1 has shown efficacy in killing cancer cells with a range of DDR gene mutations such as BRCA2 and PTEN – and importantly it does not kill cells without those mutations (i.e. healthy cells).

This could be a game changer in the oncology space

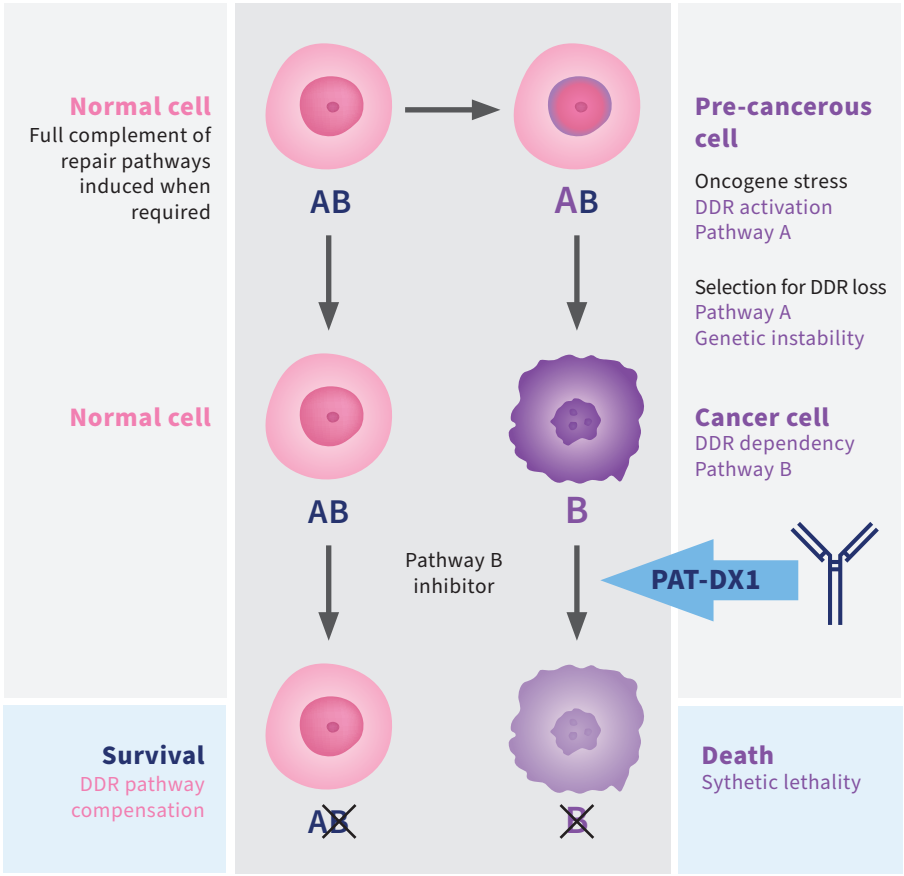
This could be a game changer in the oncology space. PAT-DX1 is the only known antibody to have shown efficacy as a single agent via the *synthetic lethality* model. Unlike other antibodies and 98% of small molecules, it can also cross the blood brain barrier (BBB), which provides all-important access to cancer cells in the central nervous system.

DDR therapeutics and synthetic lethality are well and truly in vogue. A recent article by Chemical and Engineering News provides an elegant summary of how the concept works, '*The notion of killing cancer cells by damaging their already compromised DNA should sound familiar. Chemotherapy agents do just that, but by using a sledgehammer to smash away at DNA. Because drugs that exploit synthetic lethality act with precision, they promise to be able to discriminate between healthy and diseased cells.*' Synthetic lethality exploits the fact that the presence of a mutation in a cancer gene is often associated with a new vulnerability that can be targeted therapeutically. Patrys is in a prime position to explore this capability with PAT-DX1.

Pharma giants are now prioritising the science of synthetic lethality in their oncology research and development portfolios. AstraZeneca says DDR therapeutics has potential for delivering '*…more selective, better tolerated medicines to improve survival in multiple cancers.*'

The US FDA recently approved AstraZeneca's drug olaparib for use in a sub-set of prostate cancer patients with DDR mutations, which was shown to prolong life in this clinical setting. Olaparib was originally approved as a therapy for the maintenance treatment of BRCA-mutated advanced ovarian cancer, so this approval reinforces the role of DDR therapeutics to help sub-populations of patients who don't respond to existing cancer therapies.

Synthetic lethality has also attracted a lot of deal making attention in the past few weeks. In May 2020, Bristol Myers Squibb closed a US$65M deal with Repare Therapeutics for access to its DDR technology platform, and Glaxo Smith Kline inked a deal with IDEAYA Biosciences for three discovery-stage synthetic lethality assets (US$100M upfront, US$20M equity investment, potential development and regulatory milestone payments of around US$465-485M and commercial milestones of US$475M for two of the more advanced programs). It is clear that big pharma and big biotech are increasingly compelled by the elegance of synthetic lethality and DDR therapeutic approaches for treating a range of tumours.

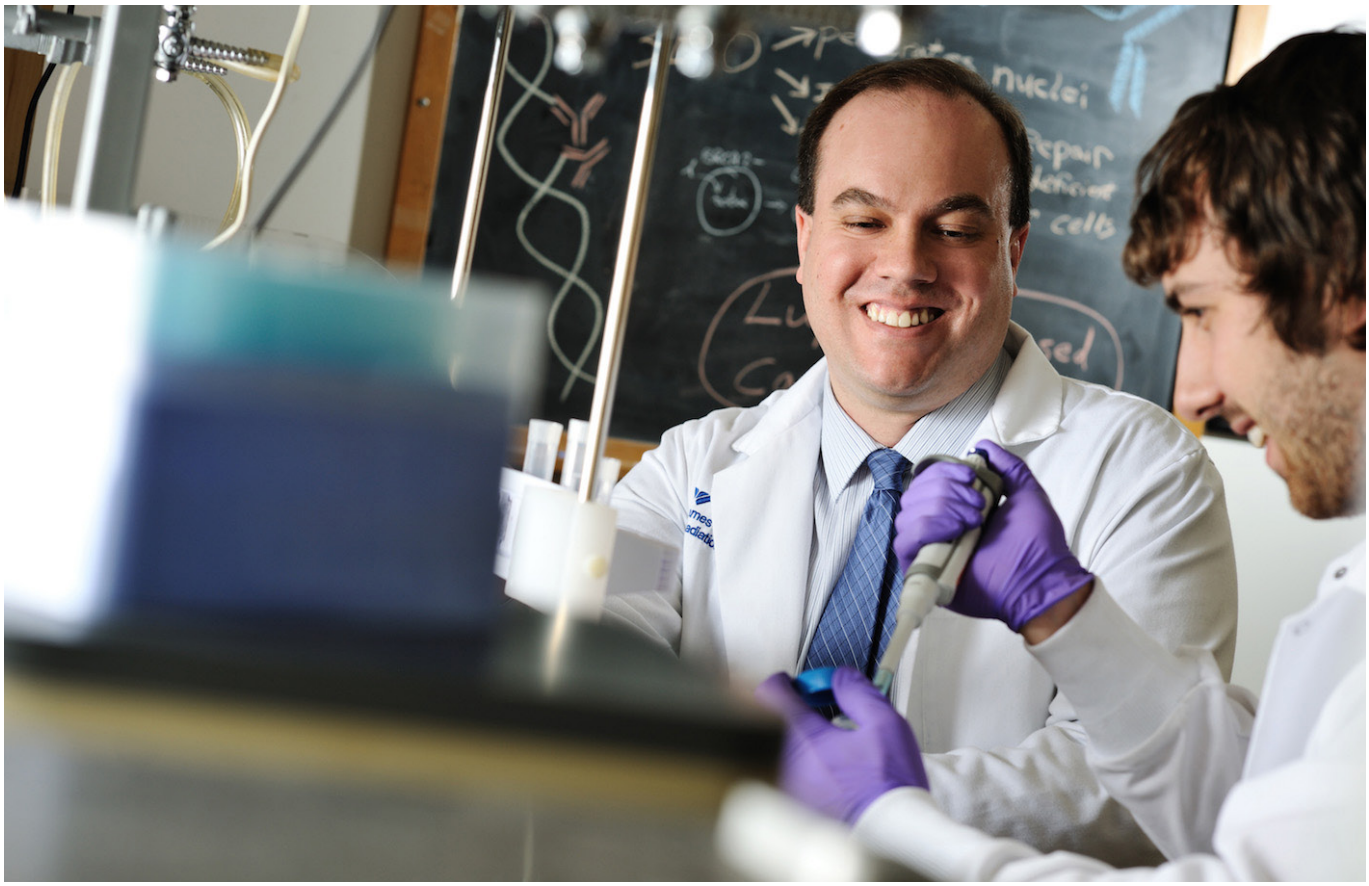


These are exciting times in the field of cancer therapeutics. Also noted by Chemical and Engineering News, many of the best known causes of cancer remain "undruggable" and researchers are struggling to develop molecules that safely disrupt their activity, but '*…researchers have long known that a cancer cell hobbling along with one broken gene is vulnerable. Knock out another key gene, they have discovered, and the cell will topple.*'

Patrys is in the enviable position of developing a novel therapeutic that combines the established safety and toxicology advantages of antibody therapeutics with the power of synthetic lethality – and it is designed to 'topple' the most stubborn, hard-to-reach cancers.

patrys

Yale researchers uncover the coveted ‘how’



Over the past two years Patrys has reported on multiple animal experiments describing the effects of PAT-DX1 on a range of brain cancers and brain metastases. PAT-DX1 has repeatedly been shown to decrease tumor size and increase survival, meaning that it must be able to cross the blood brain barrier (BBB).

Earlier this year Patrys’ esteemed research collaborators from Yale School of Medicine, Dr James Hansen and Dr Jiangbing Zhou, gained critical insights into the unique mechanism of action of our lead candidates PAT-DX1 and PAT-DX1-NP – unveiling how these novel antibody treatments can potentially target aggressive cancers.

This new data provides fundamental insight into the inner-workings of PAT-DX1, supports previously-noted evidence of its novel properties, and boosts Patrys’ broader R&D plans too.

It is well established that the human BBB prevents antibodies and the vast majority of small molecule therapeutics from entering the central nervous system – but in animal models, the team at Yale School of Medicine has shown that Patrys’ technology makes this possible.

The discovery showed mechanistically that PAT-DX1’s ability to cross the blood-brain barrier (BBB) is mediated by the equilibrative nucleoside transporter 2 (ENT2) pathway.

patrys

Drs. Hansen and Zhou completed an *in vitro* study that confirmed ENT2's pivotal role in transporting PAT-DX1 across both an animal model and a model of the human BBB, and showed that co-treatment with a small molecule inhibitor of ENT2 blocks this transport.

This confirmation of the role of the ENT2 pathway in PAT-DX1's transport across the BBB confirms an entirely new and highly effective mechanism of action that supports our plans to advance to IND filing and commence clinical studies, together with enhancing partnering discussions.

To learn that PAT-DX1 can cross the BBB is truly exciting for our supporters and potential future patients in dire need of newer, smarter treatments – and it is attracting recognition from high calibre US government funding agencies. In the past few months Dr Hansen has been awarded a prestigious A$2.85M R01 research grant from the US National Institutes of Health (NIH), a A$78,000) pilot grant from the Lion Heart Fund for Cancer Research and a A$1.95M research grant from the US Department of Defence (DoD) to fund ongoing work on PAT-DX1 and PAT-DX1-NP.

An entirely new and highly effective mechanism of action

Patrys would like to thank our research collaborators at Yale for their invaluable work to develop and refine these life-changing technologies.

Building on the grant success of our global research partners, Patrys is pleased to announce that the Olivia Newton-John Cancer Research Institute (ONJCRI), as the La Trobe University School of Cancer Medicine, has been awarded a $50,000 Federal Government grant to support research at ONJCRI on Patrys' PAT-DX1 program.

ONJCRI is one of Australian's leading biomedical research institutes with strengths in cancer biology, translational medicine and clinical trials. Patrys is delighted to establish this collaboration with Professor Robin Anderson and her team at the ONJCRI to investigate the effect of PAT-DX1 on regression of primary and metastatic breast cancers in combination with standard-of-care radio- and chemo-therapies.

Meet the team
Patrys Chairman, John Read

The role of Chairman is to promote the highest standards of probity, integrity and corporate governance within a Company.

At Patrys, we are fortunate to have a highly respected person in this role, John Read. He has extensive experience in public, private and government organisations – all with a common goal to make the world a better, healthier place.

"I have a lifelong interest in innovation and its role in improving our quality of life, creating skilled employment and exports whilst delivering material shareholder wealth," he said.

John is an experienced Chairman and Director. 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. That's ultimately why he joined Patrys.

"At Patrys, I have the ability to contribute to an organisation that is commercialising innovative antibody technologies that have the potential to revolutionise the therapeutic outcomes of a significant population diagnosed with some of the most aggressive forms of cancer."

NEW SAB APPOINTMENT

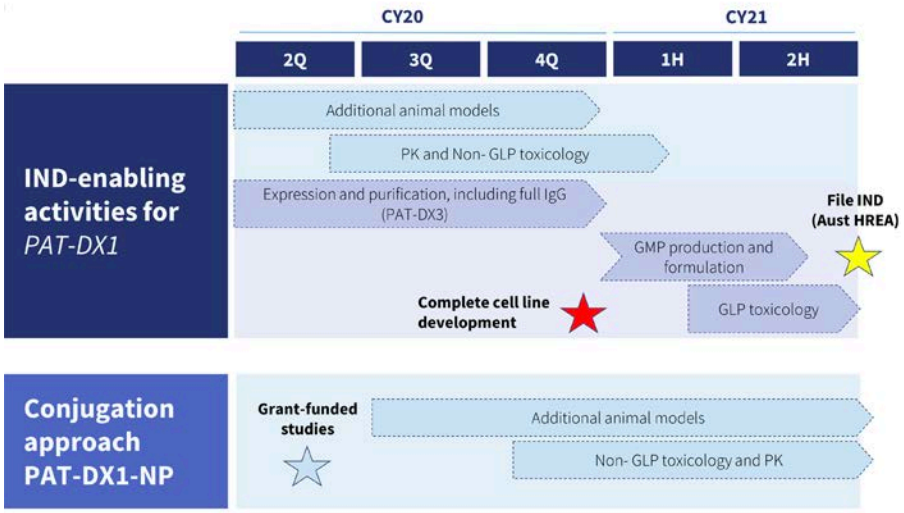
Patrys recently welcomed a highly respected and experienced US-based biotechnology executive, Dr Peter Ordentlich, to join its Scientific Advisory Board (SAB).

Dr Ordentlich has built a strong portfolio of skills in translational medicine and clinical development over the course of his career and has progressed tens of molecules, both biologics and small molecules, into the clinic.

Welcome, Peter!

Clinical development opportunities

Patrys is motivated to deliver a significant breakthrough in the oncology space. The potential for our technologies to extend beyond the initial targeted indications of glioblastoma multiforme (GBM) and triple-negative breast cancer (TNBC) is promising too.



Patrys is working systematically through the safety and manufacturing steps prior to filing for approval to conduct a clinical trial:

- Completion of non-GLP toxicology and pharmacokinetic studies by Q3 2020
- Expansion of Deoxymab platform applications (nanoparticles, alternate configurations)
- Completion of stable cell line development by Q4 2020
- Initiation of GMP production and formulation program by Q4 2020
- Initiation of GLP toxicology studies by H1, 2021
- File IND (as Australian HREA) submission in H2 2021 or H1 2022
- Phase 1 clinical trial in CY 2022

Whilst each of these outcomes moves us closer to the end goal of progressing PAT-DX1 through clinical development, there are two pivotal outcomes that dramatically reduce the risk profile of Patrys' development program for PAT-DX1. The first of these is the completion of stable cell line development, which is on track to occur in Q4 CY20. With a stable cell line, Patrys will have a pure, repeatable and reliable process for producing the PAT-DX1 antibody fragment. The stable cell line will then be used in production and purification runs of increasing size as the Company prepares for clinical development.

The second value-crystalizing outcome will be the filing and acceptance of an Australian Human Research Ethics Application (HREA) – the equivalent of a US IND. This step will be the signal that Patrys has completed all of the requite pre-clinical development work to safely commence human clinical trials. The dossier to be submitted will address all aspects of drug manufacturing and biology, from production and processing through to toxicology and tumor responses. This is a substantial body of painstaking work, and the Patrys team is diligently progressing through the required steps.

Guided by our expert Scientific Advisory Board and clinical experts we are confident that PAT-DX1 has the potential to transform cancer treatment for several tumor types for which there are currently no effective therapies.

This aspiration drives the Patrys team every day, and we look forward to sharing the journey with you.

patrys