2016 ANNUAL REPORT (EXTRACT)

patrys

Company Profile

Patrys Group is a biopharmaceutical drug development company with operations in Australia and the United States of America.

Patrys' expertise and assets target antibody therapeutics in the field of oncology with both IgM antibodies and IgG antibody fragments under development.

Patrys has successfully out-licensed a clinical candidate, PAT-SC1 for the Chinese oncology market and has conducted two clinical trials with another lead candidate from its IgM platform, PAT-SM6. Patrys has recently in-licensed from Yale University a suite of novel, nucleus-penetrating antibodies (Deoxymabs 3E10 and 5C6) which it will progress through development. Patrys will continue to advance lead candidates from both its technology platforms towards the market.

Patrys Limited is an ASX listed company (ASX:PAB) with its corporate headquarters in Melbourne, Australia.

For further information on Patrys, visit www.patrys.com

Operations

- Head Office in Melbourne, Australia
- Patrys Limited trades on the Australian Securities Exchange (ASX:PAB)

Milestones

2H 2015

- Licensing of Chinese rights for PAT-SC1
- Finalisation of strategic review of assets and capabilities

1H 2016

- Acquisition of novel nucleus-penetrating antibody assets developed at Yale University (Deoxymabs 3E10 and 5C6)
- Publication regarding Deoxymab 3E10 in *Nature Reviews Rheumatology*
- Publication of positive response of multiple myeloma patient with PAT-SM6 and other agents in *Clinical Cancer Research*

Patrys' Assets

- **PAT-SC1** is an immunoglobulin M (IgM) type antibody which targets an isoform of the membrane-bound protein CD55 (DAF). This isoform has been shown to be significantly over-expressed on the membrane of gastric cancer tissues (74%), while no expression was detected on healthy cells and tissues. In September 2015 Patrys signed an exclusive development and commercialisation license agreement for all oncology indications in China for PAT-SC1 with the Chinese company Hefei Co-source Biomedical Co.

- **PAT-SM6** is a fully human monoclonal antibody (mAb) of the IgM type which targets a variant of human GRP78 and human apolipoprotein B100 (apoB100) found in low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL). It has been successfully utilised in both melanoma and multiple myeloma clinical trials. Further clinical trials for this product candidate have been deferred due to manufacturing issues.

- **PAT-LM1** is a fully human IgM mAb that targets a variant of the human NONO protein (also named nmt55 and p54nrb), a multi-functional nuclear protein. PAT-LM1 has shown promise in a range of preclinical disease models.

- **Deoxymab 3E10** is a lupus autoantibody that penetrates live cell nuclei by binding to DNA or its precursors outside of cells and then following it into cell nuclei through a nucleoside transporter. Once in the nucleus 3E10 interferes with DNA repair processes. To prepare 3E10 for clinical development, it will be modified to remove any components that could carry a risk of causing lupus-like side effects. In addition, 3E10 will be optimised to enhance its binding to DNA and increase its effect on DNA repair-deficient cancer cells. 3E10 is currently in preclinical development.

- **Deoxymab 5C6** is another lupus autoantibody that penetrates live cell nuclei, is highly toxic to cancer cells with DNA repair deficiencies and has potential to be used in cancer therapy. 5C6 is currently in preclinical development.

Pipeline

Product *(Target)*	Discovery	Preclinical	Phase I	Phase 2a	
PAT-SC1 *(CD55)*	Gastric Cancer				**Chinese rights out-licensed**
PAT-SM6 *(GRP78)*	Multiple Myeloma				**Trial Deferred**
PAT-LM1 *(NONO)*	Solid Tumours				**Licensing candidate**
Deoxymab 3E10 *(DNA)*					**Licensed from Yale University**
Deoxymab 5C6 *(DNA)*					**Licensed from Yale University**

Letter from Chairman and CEO

Dear Shareholders,

Welcome to Patrys' 2016 Annual Report.

Patrys remains, as it always has been, a company devoted to the development and commercialisation of novel antibody technologies for the treatment of cancer. Novel therapies are desperately needed to help fight a range of different cancers, and despite some exciting developments over the past decade the need is just as great now as it was when the company was listed in 2007.

The past year has been one of consolidation and rebuilding for Patrys and its shareholders. This has meant an unavoidable period of low news flow, but the company is now well positioned to build on its assets and looks forward to sharing these developments with its shareholders over the coming year.

With the deferment of the planned phase 1b/2a combination clinical trial of PAT-SM6 in patients with relapsed and refractory multiple myeloma due to previously described manufacturing issues, the company sought to acquire and progress complementary technologies that would leverage its core capabilities, networks and alliances. After a rigorous screening process that evaluated development costs and timelines, potential value creation, intellectual property position and commercial potential the company successfully completed the acquisition of Nucleus Therapeutics, a private company with a license to novel nucleus-penetrating antibody technology ("Deoxymabs") from Yale University in the USA in March 2016.

Deoxymabs

Deoxymab 3E10 is a lupus derived autoantibody. Unlike normal antibodies that the body produces which bind to foreign cells (eg pathogens) or aberrant cells (eg cancer cells) and trigger an immune response, autoantibodies bind to normal cells. Of particular interest with 3E10 is that whilst most antibodies bind to markers on the surface of cells, 3E10 penetrates cells' nuclei and binds directly to DNA. Having bound to the DNA, 3E10 inhibits DNA repair and damages DNA. Normal cells repair DNA damage utilising intact DNA repair processes, however 3E10 can kill cells that have mutations or deficiencies in DNA repair mechanisms as found in various cancer cells. As well as showing single agent therapeutic potential 3E10 has been shown to significantly enhance the efficacy of both chemo- and radiotherapies.

Patrys believes that 3E10 and its sister antibody 5C6 may have application across a wide range of malignancies such as gliomas, melanomas, prostate, breast, pancreatic and ovarian cancers.

Significant progress has been made with the 3E10 program since it was acquired, and the company has a fully-costed development plan to progress this asset towards the clinic within the next two years.

IgM assets

The company, in conjunction with its partners is addressing the fundamental issues that arose with the manufacturing of PAT-SM6 antibody, and is seeking to progress the development of PAT-SM6 and its other IgM assets on a risk sharing basis. Cost effective solutions that leverage new technologies and learnings from other companies working in the field of IgM antibodies will be critical to advance these programs.

During the financial year, Patrys completed the out-licensing of its asset PAT-SC1 to Hefei Co-source Biomedical Co., an integrated Chinese drug development company. The license agreement covers the exclusive development and commercialisation rights for all oncology indications in China for PAT-SC1. Patrys received an up-front licensing fee, and may, pending the achievement of prescribed milestones, receive multiple milestone payments and royalties on eventual product sales.

Patrys' IgM IP portfolio continues to progress, with three patents granted in the past 12 months. As has previously been noted, Patrys' CAR-T development program performed in collaboration with a European company was completed and a decision was made that further development was not warranted. A research collaboration with Macquarie University is ongoing, and will conclude in 2017.

Looking ahead

The Patrys team is focused on progressing its new Deoxymab assets and cost-effectively developing its existing IgM assets. With tight financial control and a clear path forward management and the Board believe that the company is well situated to build value from its existing base of capital and assets and looks forward to sharing this journey with its shareholders over the coming year.

John Read
Chairman

Dr James Campbell
Managing Director and CEO

Despite recent advances, novel therapies are desperately needed to help fight a range of different cancers

The 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. He is currently the Chairman of CVC Limited (ASX: CVC) and Eildon Capital Limited and was the Chairman of Pro-Pac Packaging Limited (ASX:PPG) from 2005 to 2010, The Environmental Group Limited (ASX:EGL) from 2001 to 2012 and The Central Coast Water Corporation from 2011 to 2014.

James Campbell, PhD, MBA
Managing Director & Chief Executive Officer

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 several Australian and international biotechnology companies. Dr. Campbell was previously the CFO and COO of ChemGenex Pharmaceuticals Limited (ASX:CXS) where, as a member of the executive team he helped transform a research-based company with a market capitalization of $10M to a company with completed clinical trials and regulatory dossiers submitted to the FDA and EMA. In 2011 ChemGenex was sold to Teva for $230M. Since 2011 Dr. Campbell has assisted private biotechnology companies in Australia, New Zealand and the USA with capital raising and partnering negotiations. Dr. Campbell is a Non-Executive Director of Prescient Therapeutics Limited (ASX:PRX), Invion Limited (ASX:IVX) and Medibio Limited (ASX:MEB). Dr Campbell also sits on a number of academic and government biotechnology advisory panels.

Michael Stork, BBA
Non-Executive Director

Mr. Stork is the Managing Director of F.J. Stork Holdings Ltd., the parent entity for PNK Holdings Ltd, an original investor in Patrys. Mr. Stork was until 2004 Chairman of the Board for Dspfactory Ltd, a leading edge developer of digital signal processing (DSP) technology for various applications including hearing aids, headsets and personal digital audio players. Mr. Stork has also played key roles in the management team and the Board of Directors for Unitron Industries Ltd., a hearing aid manufacturing Company that was voted one of the 50 Best Managed Private Companies in Canada for 2000. Unitron was sold to Phonak Holdings AG, a publicly traded Swiss Company, in 2002.

Suzy Jones
Non-Executive Director

Ms. Jones is Founder and Managing Partner of DNA Ink LLC, a life sciences advisory and business development firm with clients in the United States, Germany, Israel and France. DNA Ink provides corporate strategic guidance to its clients leading to transactions that support corporate growth including licensing, M&A and fundraising transactions. Prior to starting her own firm, Ms. Jones spent 20 years at Genentech where she served in many roles including Interim Head of Partnering, Head of Business Development, Senior Project Manager and Research Associate. She managed several products during this time including Rituxan, the first monoclonal antibody launched to treat cancer. Ms. Jones has very extensive networks within the pharmaceutical and biotech companies and VC community in North America. Ms. Jones is a Non-Executive Director of Calithera Biosciences, Inc. (Nasdaq:CALA), a clinical-stage pharmaceutical company focused on discovering and developing novel small molecule drugs directed against tumor metabolism and tumor immunology targets for the treatment of cancer.

New assets licensed from Yale University

About Anti-DNA Autoantibodies

Under normal circumstances, the immune system uses antibodies to seek out and destroy invading organisms or abnormal cells such as cancer cells. To safely perform this role, it is critical that antibodies are able to distinguish between normal host cells and dangerous invading or malignant cells. To this end the immune system has evolved an elegant set of checks and balances to ensure that antibodies that might react to normal cells are eliminated before being released into the circulation. However, occasionally errant processing results in the production and release of antibodies that incorrectly recognize normal cells as being dangerous, and these antibodies then launch an assault on the host's normal cells damaging a wide range of normal tissues. These abnormal antibodies are referred to as autoantibodies, and the diseases that result are known as autoimmune diseases.

The disease systemic lupus erythematosus (SLE) is one of the most severe autoimmune diseases. A distinguishing feature of SLE is the production of autoantibodies that specifically bind to DNA (known as anti-DNA autoantibodies). These anti-DNA autoantibodies have long been considered something of a mystery, because the vast majority of DNA is housed within cells in the nucleus where antibodies were considered unable to gain access. For many years it was believed that these anti-DNA autoantibodies could only bind to the small amounts of free DNA that is present outside of cells (so-called extracellular DNA, or exDNA). However, in recent years a large body of evidence has accumulated that demonstrates that a select group of lupus anti-DNA autoantibodies can penetrate into the nucleus of living cells where they can bind to their target DNA.

This discovery raised the possibility that such autoantibodies could be used in molecular therapy techniques, in particular for the treatment of cancer. Among the many antibodies that have been considered, two stand out as having significant potential for use against cancer. These antibodies are referred to as Deoxymabs (3E10 and 5C6).

Yale University in New Haven, Connecticut

About Deoxymab 3E10

3E10 is a lupus autoantibody that penetrates live cell nuclei by binding to DNA or its precursors outside of cells and then following it into cell nuclei through a nucleoside transporter. Once in the nucleus 3E10 interferes with DNA repair processes, but the degree of inhibition of DNA repair caused by 3E10 is modest and is not enough to kill normal cells that have robust mechanisms to manage insults to DNA. On the other hand, many cancer cells are exquisitely sensitive to DNA damage because their DNA repair machinery is already impaired. When these cancer cells encounter 3E10, they accumulate more DNA damage than they can tolerate and ultimately die. 3E10 is therefore selectively toxic to cancer cells that have deficiencies in DNA repair, which includes a wide range of malignancies such as gliomas, melanomas, prostate, breast, and ovarian cancers and many others. When combined with DNA-damaging agents such as chemotherapy or radiation, 3E10 has an even greater effect on these cancer cells.

Deoxymab 3E10 is particularly well suited for use in cancer therapy because it preferentially localizes to tumors but not normal tissues. As tumors grow and go through cycles of proliferation they are constantly releasing exDNA, and this results in accumulation of a "swarm" of exDNA in the tumor vicinity. 3E10 is specifically attracted to DNA, and moreover is dependent on the presence of exDNA in order to penetrate cell nuclei. The swarm of exDNA in the tumor vicinity therefore not only attracts 3E10 to the tumor, but then also facilitates nuclear penetration by 3E10 into the tumor cell nuclei where it then inhibits DNA repair and kills the tumor cells and sensitizes them to DNA-damaging agents.

To prepare 3E10 for clinical trial testing, it will be modified to remove any components that could carry a risk of causing lupus-like side effects. In addition, 3E10 will be optimised to enhance its binding to DNA and increase its effect on DNA repair-deficient cancer cells.

Since acquiring the rights to develop and commercialise 3E10 Patrys has completed detailed in silico biology to optimise 3E10, and has entered into a sponsored research agreement with Yale University to complete lead candidate selection and pre-clinical testing. Patrys anticipates that lead candidate selection will be completed by the end of 2016, and is preparing for a suite of pre-clinical tests to be performed in H1, 2017.

3E10 Fragment

A single-chain variable fragment (scFv) is not actually a fragment of an antibody, but instead is a fusion protein of the variable regions of the heavy (VH) and light chains (VL) of antibody or immunoglobulin, connected with a short linker peptide of ten to about 25 amino acids. The linker is usually flexible and can either connect to either end of the fragments. This protein retains the specificity of the original antibody, despite removal of the constant regions and the introduction of the linker.

Patrys is in the process of constructing both di- and tri-scFv based on the parental 3E10. These molecules will be referred to as 3E10 Fragments.

About Deoxymab 5C6

5C6 is another lupus autoantibody that, like 3E10, penetrates live cell nuclei, is highly toxic to cancer cells with DNA repair deficiencies and has potential to be used in cancer therapy.

Mode of action of 3E10

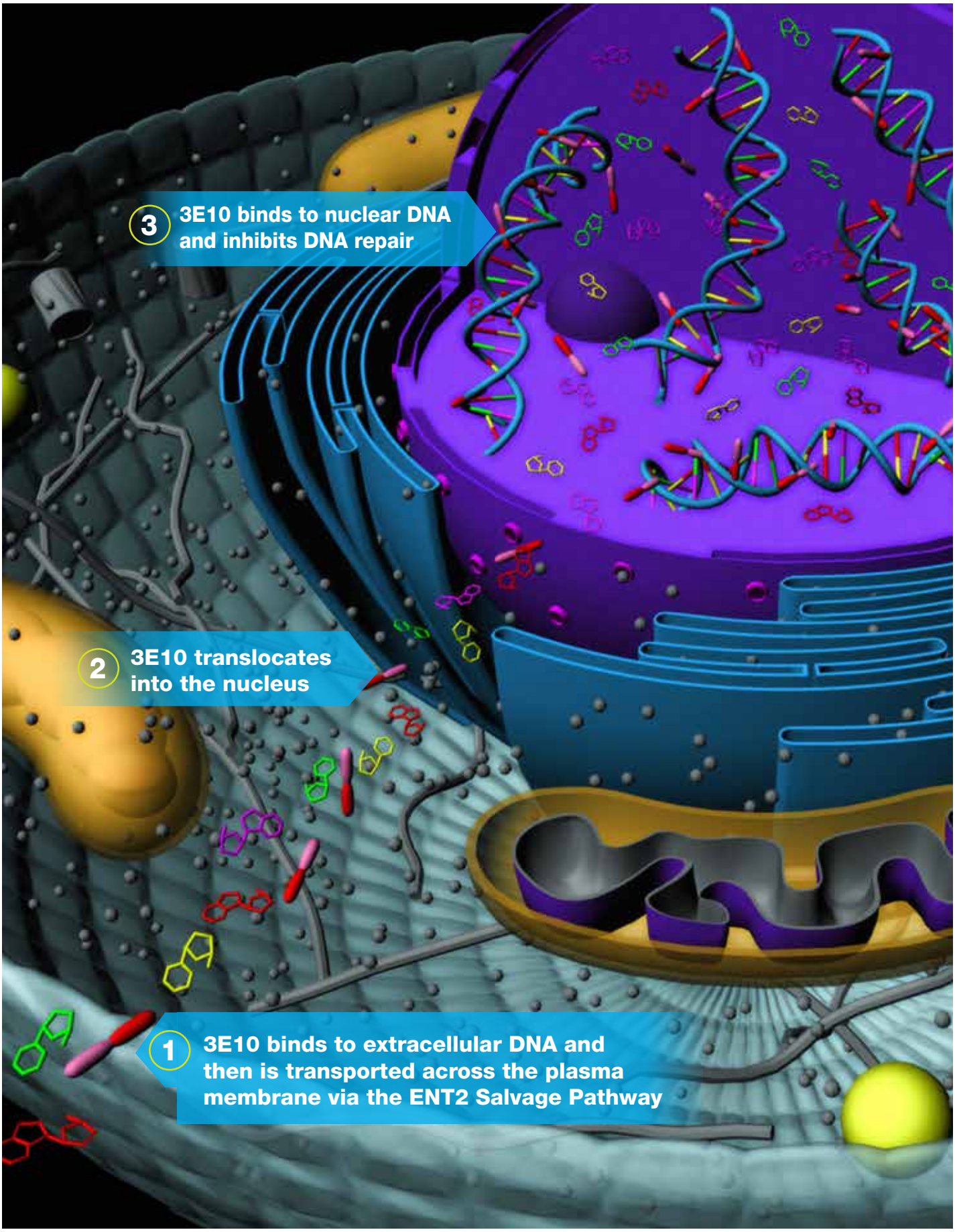

Image by www.christianchang.com

IgM Platform Update

Natural Human Antibodies to Cancer : The IgM Story

All humans generate abnormal or precancerous cells on a regular basis. However, only a small percentage of the general population develops cancer as in healthy humans the immune system constantly generates potent antibodies that seek out and kill abnormal or precancerous cells before large tumours are formed. In contrast, the elderly, who often suffer from compromised immunity, have a significantly higher rate of cancer compared to the rest of the population.

Over 99% of the anti-cancer antibodies generated by the human immune system are of the IgM subclass, and after millions of years of selective pressure and evolution, these IgM antibodies possess certain unique anti-cancer attributes including, but not exclusively:

- **High avidity** - IgM antibodies can bind to multiple copies of given targets on a cancer cell surface, leading to cross-linking and more effective cell killing.
- **Broad applications** - IgM molecules typically target a variety of conserved proteins and carbohydrates on cancer cells.
- **Safety** - Because these antibodies are generated by the human immune system, they are not likely to trigger negative immune responses.
- **Enhanced tumour cytotoxicity** - IgMs have been shown to be superior mediators of complement dependent cytotoxicity, an important effector function when fighting diseases such as cancer.

The combination of effectiveness/potency, safety, and new mechanisms for killing cancer provides a very promising profile for the therapeutic use of natural human antibodies for cancer.

Patrys' Natural Human Antibodies

Patrys' proprietary technologies cover antibody capture, screening, target discovery and large scale production.

Over 45 peer reviewed articles have been published covering IgM discovery and development technologies and the associated antibodies and targets.

A brief description of Patrys' technologies is set out below:

Antibody Capture and Screening

The first step in Patrys' approach involves the isolation from human donors of individual B-cells that produce antibodies that attack cancer tissues but ignore normal tissues. Antibodies are then selected for further development based on their anti-cancer potential as determined through an extensive array of *in vitro* and *in vivo* experiments.

Target Discovery

Patrys' approach identifies lead anticancer antibodies based on their ability to preferentially bind to cancerous cells rather than healthy tissue, then using these lead antibodies seeks to identify the target(s) on cancer cells against which the antibodies are directed.

Patrys natural human antibody platform allows it to identify candidates that have the potential to treat a number of diseases. Patrys has previously conducted clinical trials in both melanoma and relapsed multiple myeloma for its lead IgM candidate PAT-SM6. The company has a strong intellectual property position which underpins this technology platform, encompassing 34 patents across 7 patent families. In the reporting period, three patents were granted including two in the United States and one in Europe. For the PAT-SM6 LDL family the claims are directed towards methods of reducing LDL levels by administering PAT-SM6 antibody. In the case of the PAT-LM1 family the composition of matter claims are directed towards PAT-LM1 epitopes as well and method of treatment claims related to the use of the epitope to generate an immune response. Lastly, the PAT-LM1 target/variants/metastasis family includes granted use claims directed towards the use of PAT-LM1 for treating metastasis.

Manufacturing

Patrys has worked with internationally recognised partners to manufacture batches of its therapeutic antibodies over the past seven years. These processes are highly complex, with multiple potential risk points. As has been noted in several disclosures to the ASX over the past 18 months Patrys' manufacturing run of PAT-SM6 produced antibody which could not be used in the proposed combination clinical trial. The company is working with its manufacturers and partners to identify a cost effective resolution to these manufacturing challenges.

Scientific Publications on Deoxymabs 3E10 & 5C6

2016

Chen Z, Patel JM, Noble PW, Garcia C, Hong Z, Hansen JE, Zhou J. A lupus anti-DNA autoantibody mediates autocatalytic, targeted delivery of nanoparticles to tumors. *Oncotarget*. 2016, Aug 2 (Epub ahead of print)

Noble PW, Bernatsky S, Clarke AE, Isenberg DA, Ramsey-Goldman R, Hansen JE. DNA-damaging autoantibodies and cancer: the lupus butterfly theory. *Nature Reviews Rheumatology*. 2016, 12(7): 429-34.

2015

Noble PW, Chan G, Young MR, Weisbart RH, Hansen JE. Optimizing a lupus autoantibody for targeted cancer therapy. *Cancer Res*. 2015, 75(11): 2285-91.

Weisbart RH, Chan G, Jordaan G, Noble PW, Liu Y, Glazer PM, Nishimura RN, Hansen JE. DNA-dependent targeting of cell nuclei by a lupus autoantibody. *Sci Rep*. 2015, 5: 12022.

2014

Noble PW, Young MR, Weisbart RH, Hansen JE. A nucleolytic lupus autoantibody is toxic to BRCA2-deficient cancer cells. *Sci Rep*. 2014, 4: 5958.

2012

Hansen JE, Chan G, Liu Y, Hegan DC, Dalal S, Dray E, Kwon Y, Xu Y, Xu X, Peterson-Roth E, Geiger E, Liu Y, Gera J, Sweasy JB, Sung P, Rockwell S, Nishimura RN, Weisbart RH, Glazer PM. Targeting cancer with a lupus autoantibody. *Sci Transl Med*. 2012, 4(157): 157ra142.

2007

Hansen JE, Tse CM, Chan G, Heinze ER, Nishimura RN, Weisbart RH. Intranuclear protein transduction through a nucleoside salvage pathway. *J Biol Chem*. 2007, 282(29): 20790-3.

Scientific Publications on IgMs

2016

Rasche L, Menoret E, Dubljevic V, Menu E, Vanderkerken K, Lapa C, Steinbrunn T, Chatterjee M, Knop S, Düll J, Greenwood DL, Hensel F, Rosenwald A, Einsele H, Brändlein S. A GRP78-Directed Monoclonal Antibody Recaptures Response in Refractory Multiple Myeloma with Extramedullary Involvement. *Clin Cancer Res*. 2016, 22(7): 4341-9.

2015

Rasche L, Duell J, Castro IC, Dubljevic V, Chatterjee M, Knop S, Hensel F, Rosenwald A, Einsele H, Topp MS, and Brändlein S. GRP78-directed Immunotherapy in relapsed or refractory multiple myeloma- results from a Phase 1 Trial with monoclonal IgM antibody PAT-SM6. *Haematologica*. 2015, 100(3): 377-84.

2014

Loos A, Gruber C, Altmann F, Mehofer U, Hensel F, Grandits M, Oostenbrink C, Stadlmayr G, Furtmuller PG, Steinkellner H, Expression and glycoengineering of functionally active heteromultimeric IgM in plants. *PNAS*. 2014, 111(17):6263-8.

Hensel F, Timmermann W, Von Rahden B, Brändlein S, Rosenwald A, Illert B. Ten year follow up of a prospective trial for the targeted therapy of gastric cancer with the human monoclonal antibody PAT-SC1. *Oncology Reports*. 2014, 31(3): 1059-66.

2013

Hensel F, Eckstein M, Rosenwald A, Brändlein S. Early development of PAT-SM6 for the treatment of melanoma. *Melanoma Research*. 2013, 23(4): 264-75.

Rosenes Z, Mok Y-F, Yang S, Griffin MD. W., Mulhern TD, Hatters DM, Hensel F, Howlett GJ. Simultaneous Binding of the Anti-Cancer IgM Monoclonal Antibody PAT-SM6 to Low Density Lipoproteins and GRP78. *PLoS One*. 2013, 8(4):1-8.

Rasche L, Düll J, Morgner C, Chatterjee M, Hensel F, Rosenwald A, Einsele H, Topp MS, Brändlein S. The Natural Human IgM Antibody PAT-SM6 Induces Apoptosis in Primary Human Multiple Myeloma Cells by Targeting Heat Shock Protein GRP78. *PLoS One*. 2013, 8(5):1-11

Corporate Directory

Directors

Mr John Read, Chairman
Dr James Campbell, Managing Director & CEO
Mr Michael Stork, Non-Executive Director
Ms Suzy Jones, Non-Executive Director

Company Secretary

Ms Melanie Leydin

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