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Bioshares

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Edition 852

Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies

Companies covered: **AVR, CUV, MX1, NSB, PAB, tafenoquine**

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-35.8%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - May '14)	26.6%
Year 14 (May '14 - May '15)	23.0%
Year 15 (May '15 - May '16)	33.0%
Year 16 (May '16 - May '17)	16.8%
Year 17 (May '17 - May '18)	-7.1%
Year 18 (May '18 - May '19)	-2.3%
Year 19 (May '19 - May '20)	39.5%
Year 20 (May '20 - Current)	12.4%
Cumulative Gain	1124%
Av. Annual gain (19 yrs)	17.3%

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Extract from Bioshares –

Patrys – Synthetic Lethality to Kill Cancer Cells

Patrys (PAB: $0.013) is operating in a promising area of oncology, termed 'Synthetic Lethality'. It is one of four approaches to treating cancer that both GlaxoSmithKline and AstraZeneca have committed to, with recent major deals in the area by GSK and Bristol-Myers Squibb (BMS).

Patrys is a stock that is flying under the radar, quietly arranging the manufacture of its lead antibody drug candidate, PAT-DX1, ahead of preclinical toxicology and then the first clinical trial around the end of 2021. However, given the nature of recent deals, a licensing deal may be on the cards before its compound even enters the clinic.

The technology Patrys is commercialising stems from research conducted, and which continues, at Yale University. Researchers identified circulating autoantibodies from patients which lupus, which passed the cell membrane and entered the cell nucleus, with this aberrant function responsible for the manifestation of the disease.

A non-harmful antibody, Deoxymab 3E10 was isolated, with an improved humanised antibody fragment developed, PAT-DX1, which has become the company's lead drug candidate.

The features of this antibody platform are that the antibodies can penetrate the blood-brain-barrier (with glioblastoma the first likely indication), are attracted to the cancer cells due to the DNA discharge from cancer cells, have the ability to enter the cell nucleus, and are relatively harmless to normal cells, but promote cancer cell death by disrupting DNA repair in cells that already have a compromised DNA repair process (which is the nature of cancer cells).

DNA Damage Response (DDR) Pathways

Patrys CEO James Campbell said that there are five major DNA Damage Response (DDR) pathways. As cancer cells develop causing abnormal cell growth, they lose some of their DNA repair machinery in at least one of those five pathways according to Campbell.

However, "blocking an additional pathway by therapeutic means should deactivate the whole DDR system in cancer cells and lead to cancer cell death" is a process that is now referred to as 'synthetic lethality'.

The approach is not hypothetical research fancy, with PARP inhibitors, which interrupt DNA damage repair, already on the market and generating billions of dollars in sales.

Success of PARP (DDR) inhibitors

In 2019, GlaxoSmithKline acquired oncology company Tesaro for US$5.1 billion, largely for its PARP inhibitor Zejula, which was first approved by the FDA in 2017 for the treatment of ovarian cancer in patients with the BRCA mutation. In April this year, that indication was broadened to all ovarian cancers (in patients who have had a full or partial response to chemotherapy). Zejula sales last year were US$295 million.

Continued over

– Patrys cont'd

AstraZeneca sees the DDR therapy field as "an exciting area of science". Its PARP inhibitor, Lynparza (which is shared with Merck) generated sales of US$1.2 billion last year. The drug was first approved in 2014 for the treatment of ovarian cancer (in patients with the BRCA mutation). It has since gained approval for the treatment of breast, pancreatic and prostate cancers.

There is strong interest in DDR therapies, including novel DDR treatment pathways, with combinations of multiple DDR therapies an obvious pursuit. This places Patrys with PAT-DX1 in a very good position if it can complete its cell line development for manufacture and clear the preclinical toxicology program.

Recent Deals for DDR Programs

Of interest to Patrys are the early stage deals that have occurred this year in the DDR therapy space.

In June this year, GSK partnered with US biotech Ideaya paying US$100 million upfront and also invested US$20 million to access three preclinical programs from Ideaya that are using the 'synthetic lethality' approach to treating cancer (using gene-editing to fine pairs of mutations to target). The programs are three years away from clinical trials.

In May this year BMS signed a discovery deal with Repare Therapeutics from Canada which included US$65 million in upfront and equity investment and up to US$3 billion in future milestone payments and fees. Rapare Therapeutics uses a gene-based screening approach to identify synthetic lethal gene pairs in patients to achieve cancer cell destruction.

Timeline

Patrys expects cell line development to be completed by the end of this year which will allow it to then produce commercial quantities of PAT-DX1. Formal toxicology studies are expected to start in the first half of next year, ahead of clinical studies around the end of 2021.

Funding

At the end of March, Patrys had $4.7 million in cash. It is currently conducting a fully underwritten rights issue to raise an additional $4.3 million at $0.012 a share.

Pre-clinical Results with PAT-DX1

In mouse studies (conducted at the Yale School of Medicine), the company showed that breast cancer metastases could be reduced by 93% with PAT-DX1 over the control.

In a mouse glioblastoma study (also conducted at the Yale School of Medicine) it was shown that PAT-DX1 reduced tumour growth by 83% using highly aggressive human glioblastoma tumours.

The Patrys Board

The board of Patrys includes several highly experienced directors. Dr Pamela Klein was formerly VP of Development at Genentech and Suzy Jones spent 20 years at Genentech in business and product development.

Summary

Patrys is capitalised at $18 million (following the rights issue). The company will be funded to complete its preclinical development of PAT-DX1, at which point, an attractive licensing transaction is a possibility for this unique approach of synthetic lethality to destroy cancer cells.

Bioshares recommendation: **Speculative Buy Class B**

(Patrys has been added to the Bioshares Model Portfolio)

Bioshares

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Some Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Cogstate, Bionomics, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Emvision, Antisense Therapeutics, Heramed, Imugene, Exopharm, Immutep, Neuroscientific Biopharmaceuticals, Invex Therapeutics