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Companies covered: **BIT, PAB, PXS, RCE, SPL**

	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)	34.8%
Cumulative Gain	1368%
Av. Annual gain (19 yrs)	17.3%

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Bioshares

7 September 2020
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Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies

Extract from *Bioshares* –

Janssen Shows Interest in SLE Antibodies

A review paper was recently published in *Trends in Biotechnology* that discussed the emerging field of antibodies derived from patients with lupus (SLE) and their cell penetrating characteristics. This is the field that Patrys (PAB: \$0.014) is working in with its improved and humanised form of the antibody 3E10, called PAT-DX1.

The paper provided a summary of what is known about the field, but of more relevance to Patrys is the interest in this field from Janssen Biotherapeutics (Johnson & Johnson) with the five authors all being Janssen researchers.

The most data that has been developed in this field is around 3E10, and a compound called 3D8 which was discovered in South Korea and forms the basis of technology being developed by Orum Therapeutics.

Over 40 years ago, research was first published which discussed how antibodies from patients with lupus were capable of penetrating cells. The lack of sufficient imaging capabilities maintained scepticism of this phenomenon until more advanced imaging techniques were developed that could provide functional data which showed that these antibodies could enter cells (cytosolic space). It is now believed that up to 70% of autoantibodies from lupus patients bind to dsDNA.

The authors wrote: "Several new entrepreneurial companies have been funded to leverage this exciting research into the engineering of cell penetrating antibodies and to bring this technology further into the clinic."

The particular focus on the review paper was on the cell penetrating abilities of these lupus antibodies, and the potential delivery of biologic drugs into cells.

Most of Patrys' work is around the use of PAT-DX1 as a direct therapeutic in cancer treatment, rather than as a delivery vehicle for other drugs. Patrys is also working on using its antibody to deliver other potent cancer drugs to and into cancer cells using a linked nanoparticle. The company has 10 families of patents around its technology with five granted patents.

However, there remain some questions around this field, including how the 3E10 autoantibody, which has a size of around 150 kDa, passes through the ENT2 transporter which is one third its size (50 kDa). It is also unclear why some lupus antibodies, such as 3E10, move into the nucleus of a cell and others do not.

Previous Results

The way that PAT-DX1 induces cancer cell death is by a process called 'synthetic lethality' whereby the DNA repair mechanism in the cell nucleus is inhibited. With cancer cells already having a compromised DNA repair system, blocking another mechanism of repair is believed to have a terminal impact on those cells, while leaving healthy cells largely unaffected.

Cont'd over

Bioshares Model Portfolio (7 September 2020)

Company	Code	Price (current)	Price added to portfolio	Recommendation	Cap'n (\$M)	Date added
Opthea	OPT	\$2.860	\$0.160	Spec Buy A	\$770	November 2014
Volpara Health Technologies	VHT	\$1.330	\$0.375	Spec Hold A	\$332	June 2017
Somnomed	SOM	\$1.880	\$0.94	Spec Hold B	\$156	January 2011
Dimerix	DXB	\$0.740	\$0.09	Spec Buy A	\$146	December 2018
Cogstate	CGS	\$0.685	\$0.24	Spec Buy A	\$117	April 2019
Cyclopharm	CYC	\$1.365	\$1.35	Spec Buy A	\$107	September 2019
Immutep	IMM	\$0.180	\$0.320	Spec Buy A	\$88	March 2019
Micro-X	MX1	\$0.185	\$0.38	Spec Buy A	\$66	May 2017
Pharmaxis	PXS	\$0.081	\$0.260	Spec Buy B	\$32	December 2016
Acrux	ACR	\$0.170	\$0.31	Spec Buy A	\$28	July 2017
Rhinomed	RNO	\$0.080	\$0.24	Spec Hold B	\$20	Jun-19
Patrys	PAB	\$0.014	\$0.01	Spec Buy B	\$20	July 2020
Adalta	1AD	\$0.110	\$0.07	Spec Buy B	\$22	May 2020

Portfolio Changes – 7 September, 2020

IN:
No changes

OUT:
No changes

Stocks Removed from Bioshares Portfolio in TTM

Date removed	Stock
August 2020	TLX
September 2019	1AD, ALC, BCT

– Patrys cont'd

The approach of synthetic lethality is one of four main oncology R&D areas GlaxoSmithKline and AstraZeneca have committed to, with Bristol-Myers Squibb also active in the space.

In preclinical (mouse) studies, Patrys' research partners at the Yale School of Medicine have shown that PAT-DX1 could reduce breast cancer metastases by 93% over the control, and in an aggressive glioblastoma model, tumour growth was reduced by 83% with PAT-DX1, which has been developed with improved activity over the 3E10 antibody.

The review article notes that the 3E10 antibody has been tested in nine patients with a form of lupus, without side effects being observed. It is accepted also that this antibody does not cause direct DNA damage, unlike some other DNA-antibodies that have shown to be toxic.

The attributes of PAT-DX1 also include an ability to cross the blood-brain-barrier, selectively localise to cancer cells (with an attraction to the DNA that is ejected from cancer cells), penetrating the cell nucleus as well as ability to interrupt tumour cell survival using the above process.

Next Steps

The two main milestones in the year ahead for Patrys are to complete development of a stable cell line for large scale production of the antibody drug candidate (Q4 2020), manufacture GMP quality drug candidate (1H 2021) and conduct formal toxicology testing (2H 2021). If the company can successfully pass through these milestones, then securing a major commercial transaction will be the target.

Patrys is capitalised at \$20 million, holding an estimated \$7 million in cash. Last financial year, the company's research partners at Yale received US government grants of around US\$4 million to further work on the antibodies for the treatment of glioblastoma and breast cancer metastases.

Bioshares recommendation: **Speculative Buy Class B**

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, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Antisense Therapeutics, Imugene, Exopharm, Immutep, Neuroscientific Biopharmaceuticals, Invex Therapeutics, Anteris Technologies

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