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Bioshares

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

Companies covered: **CYP, PAB**

	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)	86.6%
Cumulative Gain	1931%
Av. Annual gain (20 yrs)	20.7%

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Extract from Bioshares –

Patrys Achieves Major Development Milestone

Patrys (PAB: $0.027) has completed a major milestone in the commercialisation of its unique anticancer drug assets. A stable cell line has been developed from which a consistent antibody product can now be manufactured.

The next step for the company is to scale up production of its antibody, PAT-DX1, with that material to be used in final preclinical toxicology and the forthcoming Phase I study.

Development of a stable cell line is a significant step in the development of a new antibody drug. It's a process that has taken Patrys around 18 months to complete. Antibody drug candidates require considerably more time and money to establish the manufacturing process due to the complexity of using a biological process to make the product, compared to the chemical processes used to make small molecule drugs.

The trade-off is that antibody drugs have a much higher chance of success in the clinic, due to their specific nature of action, and can command substantially higher pricing due to the cost of development and manufacture of final product.

Development of a cell line for antibody production was even more difficult for PAT-DX1 than for traditional monoclonal antibodies due to the peculiarity of action of this compound. One of appealing features of PAT-DX1 is that it is attracted to DNA which is released from dying tumour cells. However it can also bind to discarded DNA in the biologic manufacturing process which can interfere with production of material. *(According to the company, Patrys has overcome this challenge by maintaining high viability cells during fermentation to limit cell death and DNA release *.)*

Patrys has been able to achieve high yields in line with other antibodies in production, with the cell line selected from six short-listed candidates. The cell line was tested to ensure the cell penetrating and cell killing ability of the antibody was maintained.

Scale up of manufacture will be the next technical hurdle, which is expected to be less challenging than creating and selecting the optimal cell line. That is expected to be finished this half, with the last stage, and most risky traditionally, being preclinical toxicology testing.

The new version of PAT-DX1 is based on the mouse antibody Deoxymab 3E10, which has previously been in a Phase I clinical study. PAT-DX1 is a humanised version, with two copies of the 3E10 binding domain. As such, the risk of an adverse safety profile emerging in preclinical studies should be lower than for an antibody drug that includes a novel binding approach.

Phase I Study in 1H 2022

The first clinical study with PAT-DX1 is expected to start in the first half of next year in Australia (Q2). It will be a dose escalation safety study (four doses, three patients per dose) in patients* with a range of cancers, which will likely include those with metastatic triple negative breast cancer.

Continued over

Patrys has completed animal model testing (*in vivo*) with PAT-DX1 in at least five trials and in *in vitro* cell models in between 15 -20 studies with what CEO James Campbell said has been consistently impressive.

Late last year the company had a poster presentation at the San Antonio Breast Cancer Symposium from an animal model in breast cancer brain metastases. That study showed that PAT-DX1 crosses the blood-brain-barrier, suppresses growth of metastatic tumours (93% less than the control) and improved survival (45% better) with no toxicity. Most of Patrys' animal model studies have involved orthotopic grafts, whereby a human tumour is implanted into the corresponding tissue in the animal model, which should provide a stronger link to potential activity in human disease.

PAT-DX1 is derived from a lupus autoantibody that is attracted to DNA such as that discarded from damaged tumour cells, has an ability to enter the cell and cell nucleus, and interrupt DNA repair mechanisms. As such it has the potential to be effective as a broad acting anticancer treatment used both as a monotherapy where there are genetic mutations or deficiencies in DNA repair mechanisms, or in conjunction with other treatments.

In planning its clinical program, Patrys is using the expertise of one of its board members in particular, Dr Pamela Klein, who ran the clinical development program for Herceptin whilst at Genentech. With Klein, Patrys has been canvassing feedback from key opinion leaders. One of the learnings has been that in the treatment of glioblastoma. This form of cancer presents as classic glioblastoma multiforme, but there are also at least four genomic variants. The appeal of a therapy such as PAT-DX1 is that potentially it could provide an effective treatment across all types of this disease given that it can cross the blood-brain-barrier, be attracted to tumours discarding DNA, and interrupt DNA repair mechanisms across all forms of the tumours.

Summary

Patrys is capitalised at $51 million. The company held cash assets of $13.2 million at the end of last year, which should be sufficient to fund operations at least to the end of next year. By this point, some major milestones should be achieved. These include:

– Scale up of manufacture of PAT-DX1
– Completion of toxicology assessment
– Commencement of Phase I studies in patients with a range of cancers

Patrys' technology is a platform which has the potential to be of use in multiple oncology therapies. This includes as a standalone or combination therapy, but also as a way to deliver other oncology drugs into tumours. With around 60% of oncology drug deals being secured at a preclinical stage, there is the possibility that a significant transaction could be achieved by the company before Phase I trials start next year.

Patrys' platform also offers a unique approach to achieve what is termed 'synthetic lethality' which has become an area of high interest in oncology drug development in just recent years which includes PARP inhibitors. This will help attract the interest of larger partners through a licensing deal if preclinical development can be successfully completed this year.

Bioshares recommendation: **Speculative Buy Class A**

**This extract includes some minor changes/clarifications from the original article.*

PAT-DX1 Development Timeline

March 2016	Assets acquired from Yale University
April 2017	Lead candidate PAT-DX1 selected (humanised version of 3E10 antibody fragments)
September 2017	PAT-DX1 out-performed 3E10 in cell penetration and cancer cell death (colon cancer cells)
	PAT-DX1 active against 5 from 7 glioblastoma tumours removed from patients. Drug confirmed taken up in cell nuclei of glioblastoma cancer cells.
	First evidence of efficacy of PAT-DX1 in mouse model of triple negative breast cancer (TNBC)
December 2017	PAT-DX1 works in synergy with PARP inhibitor in colon and brain cancer cells, where defective DNA pathway exists, leaving healthy cells intact.
May 2018	Significantly reduced growth and viability of glioblastoma tumour spheres derived from cancer stem cells.
December 2018	In mouse model of TNBC, 93% less brain metastases with PAT-DX1 (systemic delivery), with 86% of mice alive compared to zero in control group. No toxicity from PAT-DX1.
May 2019	In animal model of TNBC, PAT-DX1 crosses BBB, achieves similar tumour growth suppression to low dose radiation therapy, and significantly more tumour growth suppression when given with radiation therapy.
July 2019	In mouse study with highly aggressive glioblastoma explant to generate brain tumours, 87% reduction in tumours when PAT-DX1 given (52% reduction from radiation therapy), and 71% survival benefit when given with radiation therapy compared to control (24% benefit from radiation therapy alone).
February 2021	Stable cell line secured
1H 2021	Manufacture scale up (to be completed)
2H 2021	Preclinical toxicology (to be completed)
1H 2021	Phase I (to commence)

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 of 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, Chimeric Therapeutics