ISSN 1443-850X

Bioshares

19 October 2018
Edition 766e

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

Companies covered: **PAB extract**

	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)	-36%
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 - current)	6.5%
Cumulative Gain	751%
Av. Annual gain (17 yrs)	17.1%

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032
Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au

David Blake - Editor/Analyst
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Editor/Analyst
Ph: 0403 850 425
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$470 (Inc.GST)
Edition Number 766e 19 October 2018)

Patrys Selects Indications for Unique Cancer Treatment Approach

In 2012, Dr James Hansen, Associate Professor of Therapeutic Radiology at the Yale School of Medicine, published an interesting finding in the field oncology which has since become the core work behind Patrys' (PAB: $0.038) therapeutic programs.

Dr Hansen was studying antibodies found in patients with lupus (systemic lupus erythematosus). In lupus, circulating antibodies, called autoantibodies, attack host DNA (including extracellular DNA). This aberrant autoimmune function is responsible for the lupus condition. Some of those autoantibodies also make their way into patients' cells and into the nucleus. The aim with Dr Hansen's work was to use these autoantibodies as cell penetrating compounds.

Dr Hansen and his team found a cell-penetrating lupus autoantibody that was not harmful to cells or tissues, called Deoxymab 3E10. This compound penetrates the nucleus via the ENT2 (equivalibrative nucleoside transporter). However, a particularly surprising outcome was that this Deoxymab E310 compound was found to have an effect on cancer cells while at the same time leaving healthy cells intact.

Cells, both healthy and malignant cells, suffer DNA damage which is repaired within the nucleus via a mechanism called DNA Damage Response (DDR). However, cancer cells have a diminished ability to self-repair and as such, are highly sensitive to additional DNA damage, which occurs in the presence of Deoxymab 3E10, causing the cancer cells to die. Healthy cells remain largely unaffected from Deoxymab 3E10.

Patrys believes that Deoxymab 3E10 preferentially accumulates at tumour cells because the dying cancer cells emit a swarm of extracellular DNA that the antibody binds to, and then makes its way into the cell nucleus.

The application of PARP inhibitors, such as Zejula, Lynparza and Rubraca, to interrupt the DNA damage repair processes in highly replicating cancer cells, has been one of several advances and breakthroughs in cancer therapies in recent years, alongside checkpoint inhibitors and Car-T therapies. Patrys' Deoxymab 3E10 technology has the potential to be added to the armoury of cancer treatments.

Lead Candidate

Through a collaboration with the Yale School of Medicine, Patrys has selected a lead candidate, PAT-DX1, which is a fusion protein (a di-single chain fragment) that is a variant of the humanised versions of Deoxymab 3E10 but with improved pharmaceutical properties.

Earlier this month, Patrys announced that it had selected a service provider to conduct the cell line development for its lead candidate, with development to start in coming weeks.

Continued over

Once that is completed, the company will need to appoint a contract manufacturer to make product for clinical studies (similar to the process Adalta is undertaking with its fusion protein).

Lead Indications - Glioblastoma & Triple Negative Breast Cancer

The company also this month announced the lead indications that it will be targeting, these being glioblastoma and triple negative breast cancer.

The company has shown that its lead compound not only penetrates the cell nucleus, but it crosses the blood-brain-barrier. It has also shown to be active against glioblastoma cells which makes glioblastoma a relevant target. The survival rate for glioblastoma is only 15 months. Standard-of-care is surgical resection, followed by radiation therapy and chemotherapy.

Patrys has previously shown that PAT-DX1 specifically targets and kills glioblastoma stem cell tumour spheres in laboratory trials (May 2018) and that a 20% improvement in survival in a mouse study was achieved in a more difficult to treat form of the disease (MGMT-unmethylated glioblastoma).

The Yale researchers have shown that its autoantibodies not only can be effective as a monotherapy, but can provide a synergistic effect when used in combination with chemotherapy or radiation therapy. Further animal data is expected to generated towards the end of this year in combining PAT-DX1 with radiation therapy and temozolomide, which will be important information on the potential of this therapy.

The other clinical program that Patrys will target is triple negative breast cancer, which is linked to BRCA mutations that make the cancers more susceptible to treatment via inhibition of DNA Damage Repair. The BRCA enzyme is involved in DNA repair. Dr Hansen has previously shown that Deoxymab 3E10 is particularly effective against BRCA2 deficient ovarian cancer cells but not against BRCA2 proficient cancer cells. It has also been shown that PAT-DX1 is effective in treating colon cancer cells that lack BRCA2 enzymes.

Future Applications

Patrys plans to apply its autoantibody technology through various approaches. This includes as a monotherapy, in conjunction with chemotherapy and radiation therapy, a nanoparticle conjugate version (which will include chemotherapy payloads attached to PAT-DX1) called PAT-DX1NP, and with another new class of DNA repair inhibition drugs, called PARP inhibitors.

Patrys recently announced that it will work with the Yale University's PET Center to gain proof-of-concept data around an imaging agent using PAT-DX1. The study will combine PAT-DX1 with the radioisotope Zirconium-89 to detect and image primary tumours and metastases for triple negative breast cancer.

Patrys' goal is to develop a companion imaging product and also a delivery construct for targeted radiotherapy (similar to Telix Pharmaceuticals), whereby PAT-DX1 will direct the radiotherapy directly to the cancer cells.

Next Steps

Following cell line development, Patrys will need to secure manufacture of Deoxymab 3E10 through a contract manufacturer. Clinical studies are expected to start in two years time. Data to monitor towards the end of this year will be animal studies in brain cancer which will evaluate the combination of PAT-DX1 with temozolomide and radiation therapy.

Summary

Patrys is operating across two areas of drug development, that of DNA damage repair, and antibody therapy technologies. It is generally accepted that antibodies are too large to block intracellular targets and bind only to targets on the outside of cells. A rare find by the researches at the Yale School of Medicine utilises the discovery of lupus antibodies that have the ability to enter cells and move through to the cell nucleus to allow selective destruction of cancer cells.

The company's share register is headed by a 9% stake held by founder investor and non-executive director Michael Stork, followed Dr Dax Calder with 8%, with the balance of the register comprising of largely retail investors. The attraction of a bluechip international biotech investor to the register is unlikely to occur until clinical studies begin to yield safety and activity data. However, some local institutions may invest in the lead up to that event. A strengthening of the company's share register by specialist institutional biotech investors would help validate the company's strategy and assets.

Given the two year time frame before clinical studies commence, Patrys is more suitable for investors with a longer term investment timeframe.

Patrys is capitalised at $41 million and held cash of $6.6 million at June 30. Its net cash spend for the year was $2.1 million.

Bioshares recommendation: **Speculative Hold 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, Bionomics, LBT Innovations, Opthea, ResApp, Pharmaxis, Dimerix, Cyclopharm, Adalta, Medibio, Pharmaust, Actinogen Medical, Patrys