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Bioshares

20 July 2020
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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Patrys – Synthetic Lethality to Kill Cancer Cells

Patrys (PAB: $0.13) 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

Anteris Technologies TAVR Advisory Board Signals High Level Interest

Anteris Technologies (AVR: $3.81) has assembled an experienced advisory board to support the company's development of its novel 3-D transcatheter aortic valve replacement (TAVR) device.

The company is currently undertaking a study in Belgium of ADAPT-treated leaflets in a valve repair trial, so far with very promising results. Anteris' tissue treatment technology addresses the calcification limitation that affects the valve leaflets made from bovine or porcine pericardium tissue. Calcification has limited the use of implantable valves in younger patients requiring heart valves, usually to address the problem of stenosis. In stenosis, valves which don't close properly cause regurgitation and degrade heart function.

The company's goal is to develop a single piece aortic valve that can be implanted using the transcatheter route, in contrast to the more invasive open surgery. The company has to date evaluated its TAVR approach in three pigs (porcine model) with data expected by year's end from a total of nine animals.

TAVR is becoming more accepted as an implantation method following the publication of several studies in recent years which have shown it to be non-inferior to surgery, and in one study (PARTNER 3) delivering lower rates of all-cause deaths, stroke, rehospitalisation and bleeding.

Medical Advisory Board

The value of medical or scientific advisory boards to small R&D companies can vary. Their value relates to not only credentials and experience of their members but more importantly how they can shape and guide a company's clinical development and commercialisation plans. Clinically active advisors may also be key opinion leaders in their own right.

Membership may or may not be compensated. If compensation is not much more than a basic honorarium, then the presence of distinguished figures may indicate a company has attracted the interest of leading researchers or physicians with a keen and genuine interest in a potentially worthwhile technology.

Members of the Anteris Medical Advisory Board are listed in the table below. Leading members include: Dr Michael Reardon, from Houston Methodist, with 55 publications relating to randomised clinical trials to his credit; Dr Samir Kapadia from the Cleveland Clinic (57 publications); and Dr Susheel Kodali from Colombia University Medical Clinic (63 publications).

Most of these advisory board members have been involved in the clinical trials of TAVR devices.

It is rare for an ASX-listed medical device company to have assembled an advisory board with this depth of experience, and is an indicator of a high degree of clinical interest in Anteris' technology.

Several members of the Anteris advisory board have discussed Anteris' ADAPT technology at recent meetings.

Cont'd over

Anteris Advisory Board			***Select Trials***			
Clinician	**Affiliation**	**Pubmed RCT Pubs**	Five-Year Outcomes of Transcatheter or Surgical Aortic-Valve Replacement	Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patient	Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients	Two-Year Outcomes After Transcatheter Aortic Valve Replacement With Mechanical vs Self-expanding Valves
Trial			*PARTNER 2*	*PARTNER 3*		*REPRISE III*
Publication			*NEJM (Feb 2020)*	*NEJM (May 2019)*	*NEJM (May 2019)*	*JAMA (Feb 2019)*
Device, Manufacturer			*SAPIEN XT, Edwards*		*Evolut, Medtronic*	*Lotus (Mechanical), Boston Scientific, CoreValve (Self-expanding (Medtronic)*
Dr Paul Sorajja	Abbott Northwestern Hospital, Minneapolis Heart Institute (Valve Science Centre)	7	Investigator		Author	
Dr Michael Reardon	Houston Methodist	55			Author	Author
Dr Samir Kapadia	Cleveland Clinic	57	Author	Author		
Dr Jeffery Popma	Harvard Medical	6			Author	
Dr Gorav Ailwadi	University of Virginia Health System	1				
Dr Susheel Kodali	Colombia University Medical Center	63	Author	Author		
Dr Vinayak Bapat	New York Presbyterian/Colombia Medical	0				
Dr Alan Zajarias	Center for Advanced Medicine, Heart and Vascular, Washington University in St Louis	23	Author	Investigator		
Dr Christopher Meduri	Piedmont Heart Institute, Atlanta	5			Investigator	Author

Bioshares Model Portfolio (20 July 2020)

Company	Code	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Opthea	OPT	$2.320	$0.160	Spec Buy A	$624	November 2014
Volpara Health Technologies	VHT	$1.400	$0.375	Spec Hold A	$349	June 2017
Telix Pharmaceuticals	TLX	$1.315	$0.910	Spec Hold A	$333	May 2019
Cyclopharm	CYC	$1.500	$1.35	Spec Buy A	$117	September 2019
Somnomed	SOM	$1.360	$0.94	Spec Hold B	$113	January 2011
Immutep	IMM	$0.180	$0.320	Spec Buy A	$88	March 2019
Cogstate	CGS	$0.405	$0.24	Spec Buy A	$69	April 2019
Dimerix	DXB	$0.340	$0.09	Spec Buy A	$67	December 2018
Micro-X	MX1	$0.165	$0.38	Spec Buy A	$59	May 2017
Pharmaxis	PXS	$0.090	$0.260	Spec Buy B	$36	December 2016
Acrux	ACR	$0.150	$0.31	Spec Buy A	$25	July 2017
Rhinomed	RNO	$0.082	$0.24	Spec Hold B	$21	Jun-19
Patrys	PAB	$0.013	$0.01	Specu Buy B	$19	July 2020
Adalta	1AD	$0.092	$0.07	Spec Buy B	$15	May 2020

Stocks Removed from Bioshares Portfolio in TTM

Date removed	Stock
September 2019	1AD, ALC, BCT

Portfolio Changes – 20 July, 2020

IN:
Patrys has been added at $0.013

OUT:
No changes

– Anteris cont'd

At the 2019 Cardiovascular Innovations Foundation meeting, Anteris Advisory Board member Dr Alan Zajarias said that "the next big advancement where valve replacement will come from is not necessarily in modifying the frames but from modifying the leaflet tissue." He said there were two advances to note including Edwards Life Sciences' Resilia and (Anteris') ADAPT. "So with these advances hopefully we will get better, longer durable valves."

https://cvinnovations.org/2019-archive/
https://www.youtube.com/watch?v=GK1GIviPCjY&feature=youtu.be

At the same meeting, a six minute presentation prepared by Dr Paul Sorajja, "Tissue Processing for Durability – A Novel TAVR", was presented by Dr Gilbert Tang in the first public presentation of the Anteris ADAPT technology used to make a single piece TAVR.

He discussed other rival alternatives in development which include Xeltis (a bio-resorbable polymer frame), Strait (a biopolymer) and the Inspirus TAVR which is made using Edwards Life Sciences' Resilia process.

Tang said that what the ADAPT processing achieved was to have residual DNA and no calcium binding sites, so preventing calcification. Other tissue methods cited which did lead to calcification included Xenosure, XenoLogiX, Photofix, Fresh BP and CoreMatrix.

He further discussed how an approach called Samurai tissue thinning could be used to thin pericardium and give the tissue a smooth, uniform thickness of 20 to 40 microns, allowing the tissue to be packed into small spaces. Samurai tissue thinning "increases pericardium yield – you don't need to buy as much pericardium – and it maintains its mechanical properties and enables 3-D molding."

Tang also said that 15 stitches were needed to attach the valve compared to 150 stitches for a current TAVR valve. The valve could also be implanted in an inverted position on a frame, which means that a much smaller dimension catheter can be used.
.
https://www.youtube.com/watch?v=yqbQTf6P-cE&feature=youtu.be

Summary

We have upgraded our recommendation for Anteris Technologies **to Speculative Buy Class B** in recognition of the interest the company has received and is likely to receive from interventional cardiologists, and also the prospects for commercial advances to take place in coming months.

Anteris Technologies is capitalised at $23 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Arakoda (tafenoquine) for SARS-CoV-2 and COVID-19 –
A Potential Treatment in the Out-patient Setting and for Post-Exposure Prophylaxis

US specialty pharmaceutical company Sixty Degrees Pharma has released preclinical data which shows the effects of its aminoquinoline compound Arakoda (tafenoquine) against the coronavirus SARS-CoV-2.

Arakoda (tafenoquine) is an 8-aminoquinoline whereas Plaquenil (hydroxychloroquine) (HCQ) is a 4-aminoquinoline.

HCQ is being evaluated in 195 clinical studies, planned or underway for the treatment of SARS-CoV-2 infection. A feature of HCQ is that it is administered orally.

Tafenoquine was approved in the USA in 2018 as a prophylaxis for malaria. Its brand name in Australia is Kodatef.

Tafenoquine is formulated as a 100mg tablet. Prior to travel into areas in which malaria is common, a patient receives 200mg once daily for three days as a loading dose, followed by a 200mg weekly dose while in an area with malaria, and then a terminal dose of 200mg seven days after leaving the area.

The drug is contraindicated for patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency and patients with psychotic disorders or symptoms.

It has also been established that tafenoquine has a low cardiotoxicity risk, which is an issue for HCQ.

Results from Evaluations

Sixty Degrees began its testing in Australia at 360BioLabs in March after being gifted SARS-CoV-2 samples [SARS-CoV-2-Australia/VIC01/2020] for testing from The Peter Doherty Institute for Infection and Immunology (the Doherty Institute), with studies being completed in early July.

The studies showed that tafenoquine demonstrated low micromolar potency against SARS-CoV-2 and was approximately four times more potent than HCQ.

An arguably more important finding was that tafenoquine has a different mechanism of action to HCQ (and also remdesivir), acting late in the viral replication cycle in the release phase.

Australian Connection

Sixty Degrees is linked to Australia through a directorship held by Jennifer Herz from (Biointelect and Biocelect). Biocelect holds the Australian distribution rights for tafenoquine. Sixty Degrees has completed one clinical trial in Australia and has a long-term safety study underway in Perth.

Funding Objective

Sixty Degrees is seeking funding and research partners to further the clinical development of tafenoquine for use in mild-to-moderate COVID-19 cases and as a prophylactic in the post-exposure setting.

High Level of Interest in Potential SARS-CoV-2 Inhibitors

There is a high level of interest in potential SARS-CoV-2 inhibitors, with Recce's (RCE: $1.36) share price having increased 423% since March 31, 2020, with recent gains being driven by a compound RECCE 327 being accepted into a screening program at the CSIRO and the Doherty Institute. Recce is capitalised at $196 million.

Summary

An orally available, less toxic, potent and selective SARS-CoV-2 inhibitor, that has already been approved by leading drug regulators for malaria prophylaxis, is an attractive investment opportunity because its different mechanism-of-action to other aminoquinoline inhibitors may strengthen global capabilities needed to address potential resistance of SARS-CoV-2 to HCQ as well as remdesivir.

Bioshares

Stock Briefs

Clinuvel Pharmaceuticals Develops Liquid Formulation of Afamelanotide

Clinuvel Pharmaceuticals (CUV: $23.40) has developed a new formulation of its drug Scenesse (afamelanotide). Scenesse is delivered in a solid form as a depot injection lasting two months. The new liquid formulation will presumably be injected.

Afamelanotide has a half-life in circulation of around 40 minutes. The new forumlation, called Prenumbra, will be used to tackle other diseases/disorders, including vascular abnormalities and conditions involving excess fluid build-up in life threatening disorders, as part of its strategy that had been in the planning for 10 years according to the company's Director of Global Operations, Lachlan Hay.

The aim with the new formulation is to provide greater flexibility in treating different conditions with a drug that now has a very safe track record from use in over 10 years in 1,400 patients. It also provides life cycle management for Scenesse.

Bioshares recommendation: **Hold**

NeuroScientific Biopharmaceuticals Adds Positive Preclinical MS Data

NeuroScientific Biopharmaceuticals (NSB: $0.22) has released additional positive preclinical data for its neuro-regenerative drug candidate, EmtinB. The company had previously shown positive results in glaucoma in pigs and in a multiple sclerosis (MS) *in vitro* model.

An extension of that MS study has now shown that not just the level of the precursor cells to myelin sheath formation, oligodendrocytes, can be stimulated with EmtinB, but that the area of myelin sheath that protect the nerve fibres can be increased significantly in a dose dependent manner over the control. CEO Matt Liddelow stated that there are currently no therapeutics available for MS that can regenerate the myelin sheath surrounding nerves.

Bioshares recommendation: **Speculative Buy Class B**

Micro-X Receives Early Approval for Rover Mobile X-ray Instrument

Micro-X (MX1: $0.165) filed its second x-ray instrument, the Rover for military use, for approval last month and received clearance to sell the instrument in the US in just five weeks.

This opens up the opportunity for early orders from the US Army, Navy and Air Force. These will be direct sales so margins will be substantially higher for Micro-X. The Rover is a more rugged version of its hospital x-ray system, the Carestream DRX Revolution Nano, which is sold by Carestream. Whilst there is central purchasing in the US military, demonstrations will need to be made to multiple groups.

Direct sales of the Rover allows Micro-X to better control the sales and marketing through a narrower distribution channel to military organisations. Micro-X estimates the market for military applications at over $170 million. Micro-X CEO Peter Rowland is seeking to sign multiple year contracts with military groups.

Having gained US clearance, the company can deploy demonstration units in the US with these units now under construction in Adelaide. However, there will be challenges in demonstrating units during the current coronavirus pandemic.

Micro-X has had a very strong year so far with high orders for its Nano instrument from healthcare groups around the world for assisting in the diagnosis and progression of disease in COVID-19. To the end of May the company had built and shipped $2.2 million worth of Nano instruments. Micro-X's current manufacturing capacity is between five to six units a week, which is expected to increase to eight units a week by August. We estimate the company has built around 200 units to date.

Market penetration and acceptance of the instrument from the emergency use to diagnose and manage COVID-19 should assist the company with sales of the Rover to military groups around the world.

The company is also seeking approval for the Rover in Australia and Europe, with interest from the UK military (and a potential procurement order later this year), and from the Department of Defence in Australia (through a tender sales process underway which is expected to be executed this year).

A high powered generator for the following version, Rover Mark II, is in development and is expected to be completed in 2021.

Bioshares recommendation: **Speculative Buy Class A**

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

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