ISSN 1443-850X

Bioshares

22 September 2021
Edition 902

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

Companies covered: **CGS, NEU OPT, PAB, RNO, SOM,**

	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 - May '21)	86.8%
Year 21 (May '21 - Current)	19.6%
Cumulative Gain	2333%
Av. Annual gain (20 yrs)	20.7%

Individual Subscriptions (24 issues/year)
$550 (Inc.GST)
Edition Number 902 (22 September 2021)

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence No. 258032

Mark Pachacz - Editor/Analyst
Email: mark[at]bioshares.com.au
Ph: 0403 850 425

Under the Radar

Whilst more than two thirds of biotechs experienced share price gains last financial year and one quarter of stocks in the sector doubled in price, there remain some quality companies that are flying under the radar, offering very good investment potential. Two of these stocks are covered below.

Opthea - Strong Gains for the Patient Investor on Offer

One of blue chip drug development companies in the sector is Opthea (OPT: $1.265), which is developing an improved treatment for wet AMD. Opthea currently has two global Phase III studies underway which will seek to recruit around 2,000 patients.

If the trials are successful, on offer is a portion of the US$10 billion plus ophthalmology market that is serviced mainly by three drugs - Eylea, Lucentis and Avastin.

In October last year Opthea raised US$119 million through a US listing. Since then its share price has almost halved. However the company's clinical trial progress is on track, and the company finished June with US$138 million in current assets (which includes US$14.4 million in prepayments for clinical trials in this financial year).

The Phase III studies started in March this year and it's expected to take 18 months to complete recruitment (September 2022) with patients to be treated for 12 months (to September 2023). The main risk between now and that time is delays in recruitment.

CEO Megan Baldwin said that so far recruitment is proceeding as expected. Interactions with regulatory agencies are proceeding as planned and all of the logistical staff are in place. European recruitment, when it opens, is expected to quick believes Baldwin. Opthea

Continued over

Amplia Therapeutics to Start Two Phase II Studies in 2022

Amplia Therapeutics (ATX: $0.185) is a stock that is flying under the radar. The company has a novel small molecule drug candidate, AMP945, that acts as an antifibrotic agent. In Q1 next year the company plans to start a Phase II study in prostate cancer in Australia, with a second study scheduled to start later in the year in the lung disease idiopathic pulmonary fibrosis (IPF).

Amplia has completed a Phase I study with the drug candidate in 56 healthy volunteers. The small molecule was found to have a very good safety profile with most side effects mild, some moderate side effects and no major side effects.

That the drug has such a favourable safety profile is allowing the company to start a Phase II study in patients with pancreatic cancer as a first line therapy, added to standard-of-care. The benefit in treating earlier stage patients is that there is a better possibility of achieving a positive efficacy signal, compared to patients who are more progressed, and recruitment should be easier.

Cont'd on page 5

has a good track record with progressing its drug trials; its Phase IIb wet AMD study in 366 patients completed recruitment ahead of schedule.

The impact of COVID-19 has been factored into the recruitment timeline which Baldwin says was set with conservative expectations.

Once recruitment is completed or nearing completion next year, we expect the company will be in a position to focus on progressing commercial discussions. Strategic discussions at the board level are now underway Baldwin said.

Those discussions may include securing a regional licensing deal for the rights to the technology with a major upfront cash payment. The wet AMD drug space is likely to be very receptive to regional deals due to the way commercial rights to drugs on the market have been assigned.

US sales rights to Eylea and Lucentis are held by Regeneron and Roche respectively; ex-US rights to Lucentis are held by Bayer and Novartis. In 2014 Novartis licensed the ex-US rights to a Phase III compound in development by Ophthotech in a US$1 billion deal with US$330 million in upfront and short-term payments. (That drug candidate subsequently failed in a Phase III study.)

First Biosimilar Approved for Wet AMD in the US this Week

There are also biosimilar manufacturers of Eylea and Lucentis that may be interested in competing with the four companies above by combining their biosimilar with Opthea's drug candidate OPT-302. This week the first biosimilar in this drug class, for Lucentis, was approved by the FDA. The biosimilar was developmed by Biogen and Samsung BioEpis. The two companies also have a biosimilar in development to Eylea.

Baldwin believes that the arrival of biosimilars to Eylea and Lucentis will work in Opthea's favour as there will be less pricing pressure. With generics lowering the price of the therapy, payment/reimbursement for an additive treatment to Eylea and Lucentis will be more affordable.

Positive Interactions with FDA

Opthea has gained several favourable decisions from the FDA for the development of OPT-302. This includes the Fast Track approval designation for Opthea's therapy which was granted by the regulator in July this year. This allows the company to submit is drug application for approval in parts under a rolling review (e.g. submission earlier of a manufacturing dossier.)

Other very important approval and trial structures include the company being able to file once top line data is received at the end of 2023, and that the two Phase III studies are comparing OPT-302 being used as a combination therapy with Eylea in one study and with Lucentis in the second study.

Opthea's initial analysis will also be in a patient sub-group (around 80% of patients) who responded better to treatment in the Phase IIb study (those with minimally classic or occult lesions) with overall results from all comers to be assessed later. This improves the probability of achieving a statistically significant result against Eylea, Lucentis or both. In the Phase II study, an overall improvement in vision of 16.1 letters was achieved in this patient sub-group with a 5.7 letter improvement over Lucentis in the combination therapy (OPT-302 plus Lucentis).

Summary

Baldwin said that the biggest challenge for the company is in completing the trial, however with a big study such as this, a big pay off can be expected (if all goes well).

Investors prepared to accumulate this stock and be patient can expect to be very well rewarded with a lower risk profile for Opthea than many other drug development stocks.

Opthea is capitalised at $440 million.

Bioshares: **Speculative Buy Class A**

Bioshares

Biosimilars to Eylea and Lucentis

Companies	Biosimilar to	Region	Status
Biogen & Samsung BioEpis	Lucentis	USA	Approved (Sept 2021)
Biogen & Samsung BioEpis	Lucentis	Europe	Approved (Aug 2021)
Xbrane Biopharma	Lucentis	Europe	To file Q3 2021
Xbrane Biopharma	Lucentis	USA	To file Q4 2021
bioeq & Coherus Biosciences	Lucentis	USA	Filed (Aug 2021)
bioeq & Teva	Lucentis	Europe	Launch in 2022
bioeq (licensed from Santo Holding)	Eylea	USA	Launch in 2024
bioeq (licensed from Santo Holding)	Eylea	Europe	Launch in 2025
Sandoz	Eylea	-	In Phase III
Amgen	Eylea	-	In Phase III
Biogen & Samsung BioEpis	Eylea	-	In Phase III

Rhinomed Secures Second Major Order for Nasal Swabs

Rhinomed (RNO: $0.36) has secured an order from the Victorian State Government (Victorian Department of Health) for one million of its nasal swabs that will be used for coronavirus testing.

This follows on from an order last month from NSW Health Pathology for the same number of swabs. The value of the latest order is between $1.4 - $1.8 million. Rhinomed CEO Michael Johnson is seeking to build up repeat business with these early customers.

Over 34 million swabs have been taken in Australia since the outbreak of the pandemic and 500 million coronavirus tests have been conducted in Europe over the same period. Johnson believes Australia is a great entry market for the company with an emphasis now on scale-up.

The swabs for both government orders are expected to be filled in the next eight weeks. The company expects to double its local manufacturing by October with additional equipment orders, including injection moulding tools, already placed. The company is also looking to install a manufacturing facility overseas.

Having secured orders from two government customers should help generate additional orders for its swabs, both in Australia and internationally.

The company also announced that it had installed a distributor for Belgium, the Netherlands and Luxembourg for its swabs (BioTrading Benelux BV) and a distributor in Western Australia (Antimicrobial Technologies Group). The link with the Benelux distributor was made through a clinical study underway in the Netherlands with the company's 'Rhinoswab'.

The Rhinoswab offers multiple benefits to the nasopharyngeal swabs without compromising accuracy and is a unique approach to testing (see previous edition). The swab is used for either antigen-based tests or PCR tests.

This new product was registered for use in the US and Australia in November last year and gained European CE Mark clearance in May this year.

A major market opportunity is currently available to Rhinomed for this new product. Its main challenge is to scale up production rapidly to service the expected demand.

Rhinomed is capitalised at $91 million with $2.4 million in cash at the end of last June.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Somnomed - Major Technology Investment for Long Term Growth

Somnomed (SOM: $2.30) believes it has moved through the worst of the pandemic conditions and is now in the 'managing COVID' phase. In FY2021, sales increased by 9% to $62.7 million with a net loss similar to the previous year at $1.2 million.

The company is making a heavy investment in technology innovations which this year will total around $8 million. The company expects to record a breakeven EBITDA this year before rebounding in 2023.

The nature of Somnomed's technology innovation remains undisclosed, with the two major innovations to be released early next year. The investment in these new technologies commenced around 18 months ago. The outcome is that the company is seeking to maintain a leading position in the oral appliance sector for the treatment of sleep apnea.

CEO Neil Verdal-Austin said that the new innovations will drive acceptance and adoption of the company's products. We expect the innovations will be around the monitoring of treatment efficacy and compliance. The role for oral appliances for sleep apnea treatment is for those patients with a mild-moderate condition, with arguably CPAP (ResMed and others) more suitable for people with severe sleep apnea.

Somnomed is planning to launch a major European/US study to compare its Somnodent Avant product with CPAP treatment. That study will see patients receive both therapies with a washout period in between. It is expected to provide information in the short-term towards the end of next year, as well as monitoring patients over the long term for compliance.

Somnomed has made extremely good progress in European markets. In France the company is generating 40% plus growth which Verdal-Austin believes comes not just from increasing adoption of oral appliances for sleep apnea, but also from taking market share away from Narval (ResMed).

Somnomed is valued at $190 million with $21.4 million in cash at the end of June.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Gates Highlights Cogstate Technology

Cogstate (CGS: $2.38) is operating in the right place at the right time. The company provides cognitive testing in the clinical trials space, with around 70% of its revenue from Alzheimer's disease drug trials. It has also moved into providing its tests to the broader population, with a global US$45 million deal last year with Eisai Co. Ltd.

With the first disease modifying Alzheimer's disease drug approved this year and launched in the US, Aduhelm from Biogen and Eisai, demand for its tests can be expected to grow significantly; not just as an aid for clinicians prescribing Aduhelm, but also by the general population to monitor cognitive health. Eisai is due to launch Cogstate's test in the US and other parts of Asia this year. (The test has been in use in Japan through Eisai for 18 months.)

This week the Cogstate technology was highlighted by Bill Gates as a tool for tackling Alzheimer's disease. "If we want to stop Alzheimer's, one of the biggest things we need to develop is a reliable, affordable and accessible diagnostic." Gates also discussed a blood-based test for beta-amyloid (which presumably correlates with amyloid plaque in the brain) being developed at the University of Gothenburg in Sweden, as well as a novel retina scan for the disease which is being explored at the University of Washington in Seattle. Gates believes that a cognitive test would be required first before confirmation of disease with a blood-based test. Gates has a strong personal interest in the area with his father succumbing to the disease.

The same driver exists for the Dolby family with the inventor of Dolby NR noise reduction system, Ray Dolby, also dying with the disease. His family is committed to accelerating therapies for tackling the disease. The Dolby family holds a 15% stake in Cogstate.

Cogstate has cemented a central position in the Alzheimer's disease drug development and management sector with its diagnostic expertise. The company is part of the recently formed Davos Alzheimer's Collaborative (DAC). It is part of the DAC Leadership Group (which includes the CEOs of Eisai and Biogen, the CSOs of Johnson & Johnson and Eli Lilly and two former FDA Commissioners), and also has representatives in the three working groups at DAC.

With Eli Lilly expected to file its plaque busting Alzheimer's disease drug candidate, donanemab, later this year for approval with the FDA, the level of activity in Alzheimer's disease trials and treatments can be expected to continue to build momentum. Cogstate is now well positioned to benefit from these major sector drivers.

Cogstate is capitalised at $407 million with US$23.6 million in cash at June 30.

Bioshares recommendation: **Accumulate**

Bioshares

Neuren Raises $20 Million and Files First IND for Second Compound

Neuren Pharmaceuticals (NEU: $2.05) has raised $20 million in a private placement at $2.05 a share and plans to raise a further $2 million through an SPP (Share Purchase Plan).

The capital raise is ahead of the release of Phase III study results later this year from its lead program, with trofinetide, which has been licensed to Acadia Pharmaceuticals for the North American region.

Neuren's second compound in development is NNZ-2591. The company is seeking to commence three Phase II studies with this drug candidate this year in orphan diseases, those being Angelman syndrome, Phelan-McDermid syndrome and Pitt Hopkins syndrome.

It's a sensible raise, giving the company a pro-forma cash balance (at 31 July) of $37 million. Whilst the additional cash will be used to fund a fourth Phase II study in a new indication, Prader-Willi syndrome (due to start mid 2022), as well as prepare for Phase III studies with NNZ-2591, the funds also deliver the company a greater buffer should the trofinetide study not meet its end points.

This week the company announced it had filed an IND (Investigational New Drug) application with the FDA for the Phelan-McDermid study with an IND for Angelman syndrome filed earlier this month. This leaves two additional INDs to be filed. The Phase II studies will be conducted in the US except for the Angelman syndrome study which will be run in Australia.

Neuren is capitalised at $255 million.

*Bioshares r*ecommendation: **Speculative Buy Class A**

Bioshares

Patrys Demonstrates Success with PAT-DX3 Drug Conjugate

Patrys (PAB: $0.04) continues to make progress with its unique cancer antibody delivery technology. Its lead compound PAT-DX1 is moving into clinical studies next year as a treatment for solid tumours. However its follow-up compound, PAT-DX3, is being positioned as a drug delivery vehicle as well for other oncology drugs.

PAT-DX3 is a full antibody version of the lead compound. Being larger in size makes it easier to conjugate (attach) other cancer drugs to it. Recently Patrys showed that this larger drug candidate can also cross the blood-brain-barrier in a preclinical model. Last week the company showed that PAT-DX3 can be attached to the cancer drug MMAE and inhibit tumour growth.

A combination of PAT-DX3 conjugated to the cancer drug MMAE reduced tumour inhibition by 99.7% after 21 days (in a xenograft

Continued over

Bioshares Model Portfolio (22 September 2021)

Company	Code	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Clinuvel Pharmaceuticals	CUV	$41.94	$20.31	Hold	$2,072	November 2020
Opthea	OPT	$1.265	$0.160	Spec Buy A	$440	November 2014
Immutep	IMM	$0.510	$0.320	Spec Buy A	$434	March 2019
Cogstate	CGS	$2.380	$0.24	Buy	$407	April 2019
Micro-X	MX1	$0.290	$0.38	Spec Buy A	$133	May 2017
Dimerix	DXB	$0.275	$0.09	Spec Buy A	$85	December 2018
Cynata Therapeutics	CYP	$0.530	$0.70	Spec Buy B	$76	December 2020
Patrys	PAB	$0.040	$0.013	Spec Buy B	$72	July 2020
Pharmaxis	PXS	$0.125	$0.260	Spec Buy B	$57	December 2016
Acrux	ACR	$0.120	$0.31	Spec Buy A	$34	July 2017

Stocks Removed from Bioshares Portfolio in TTM

Date removed	Stock
September 2021	LBT
July 2021	1AD
June 2021	CYC
October 2020	RNO, SOM, VHT

Portfolio Changes

IN:
No changes

OUT:
We have removed LBT to lock in some profits after an 86% gain.

– Amplia cont'd from p1

Strong Preclinical Data in Pancreatic Cancer Model

AMP945 is a FAK (focal adhesion kinase) inhibitor which is implicated in the fibrotic pathways in the body. That the compound is an anti-fibrotic and not an anti-cancer compound helps explain its more benign safety characteristics. In a mouse model (KPC) of pancreatic cancer conducted at the Garvan Institute in Sydney, which is a highly aggressive and difficult model to treat, a 25% improvement in survival was achieved against standard treatment which Professor Paul Timpson said was "…very impressive and a level of improvement that we rarely see."

FAK Helps Build Fibrotic Network Around Tumours

FAK is found to help stromal cancers such as pancreatic cancers survive and resist treatment by building and maintaining a dense, fibrotic tissue around the tumours. The aim with an antifibrotic compound (similar to that being developed by Pharmaxis) is to attack the fibrotic network to allow existing oncology drugs to take effect.

Increased levels of FAK is linked to many difficult-to-treat tumours. FAK is also believed to suppress the immune system and regulate (assist) cancer metastases.

There are two other FAK inhibitors that are in development. One is from Verastem (defactinib) and the other is from InexMed (IN10018). Amplia's drug candidate has shown to have greater selectivity than the competition, which means a stronger dose can be given with less off-target binding.

Strong Board and Management Team

Amplia has a strong management team and board. Its CEO is John Lambert (formerly at Biota Pharmaceuticals), and Mark Devlin is the CSO (formerly at the Peter MacCallum Cancer Centre). The board includes Robert Peach (co-founder of Receptos which was sold for US$7.8 billion), Warwick Tong (former CEO of Cancer Therapeutics CRC) and Christopher Burns (formerly head of medical chemistry at Cytopia).

Summary

The strong safety profile of AMP945, its highly specific binding nature to the target, as well as the ability to be delivered orally has the potential for the compound to become an effective combination therapy in very difficult-to-treat stromal cancers such as pancreatic and ovarian cancer, as well as the potential long term use in fibrotic diseases such as IPF.

Amplia Therapeutics is capitalised at $23 million with $4.1 million in cash at the end of June. Another capital raise will likely be required before the Phase II studies commence.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

– Patrys cont'd from previous page

model of a breast cancer cell line), with MMAE conjugated to a control antibody having substantially lower inhibition according to CEO James Campbell. (MMAE can not be delivered on its own due to its high toxicity.)

The next challenge for the technology is to see if PAT-DX3 conjugated with other cancer drugs can be delivered across the blood-brain-barrier.

Patrys is capitalised at $72 million.

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 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, Antisense Therapeutics, Imugene, Exopharm, Immutep, Neuroscientific Biopharmaceuticals, Invex Therapeutics, Anteris Technologies, Chimeric Therapeutics, Neuren Pharmaceuticals, Neurotech International

Subscription Rates (inc. GST)

24 issues per year (electronic distribution): **$550**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:

$900	2-3 email addresses
$1200	4-5 email addresses
$1500	6-10 email addresses

To subscribe, post/email this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
info@bioshares.com.au

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

The information provided in Bioshares, including general investment advice, is provided only for receipt and use in Australia and New Zealand, for subscribers to Bioshares, who are Australian or New Zealand citizens or commercial entities.