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Companies covered: CGS, CUV, DXB, IMM, IMU, MSB, MX1, OPT, PAB, PYC, RAP, TLX, Ellume, Planet Innovation

	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)	8.0%
Cumulative Gain	2097%
Av. Annual gain (20 yrs)	20.7%

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Bioshares

25 August 2021
Edition 900

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

Bioshares Special Edition

Top 10 Events in Australian Biotech in the Last 100 Editions

In the 900th edition of Bioshares, we take a look at the most important listed and private company events in Australia's biotech industry over the last two years.

The worldwide pandemic has brought biotech to the fore with ways to combat the SARS-CoV-2 virus that has caused severe global disruptions. The importance of biotech has accelerated and intensified investment interest in the sector as a result. In 2020, $1.7 billion was raised by listed companies, up 62% over the previous year. In FY2021 68% of companies experienced share price gains with 25% of companies more than doubling over the year.

Below we list the 10 most significant events in Australia's biotech sector in the last 100 editions of Bioshares.

1. Clinuvel Pharmaceuticals - FDA Approval and Fully Integrated Vision for Scenesse

In October 2019, Clinuvel Pharmaceuticals achieved a very rare feat for an Australian biotech – bringing a drug through all stages of development and culminating with FDA approval. Clinuvel has built a fully integrated pharmaceutical company from scratch, controlling manufacturing, sales, marketing and distribution throughout Europe, the US, Australia and other regions. The company is now seeking to leverage that asset by investigating other applications of the same active drug and from product variations.

Its net cash from operations last year was $19.3 million and the company holds a healthy $83 million in funds.

2.Opthea - Raises $180 Million and Launches Global Phase III Trials in Wet AMD

Opthea announced in August 2019 that it successfully met its primary endpoint with its drug candidate OPT-302 for the treatment of wet AMD. It is a massive market opportunity for the company with the two leading drugs generating sales in excess of US$10 billion a year.

The company then went on to raise $50 million at the end of that year, followed by a $180 million capital raising through a US IPO. In March, Opthea started two global Phase III studies in wet AMD that will recruit around 2,000 patients.

Continued over

Whilst the company's share price has halved since its US listing, it offers a very attractive investment to patient investors. The primary completion date for the study is December 2023.

3.Telix Pharmaceuticals - US$50M Upfront Licensing & Investment Deal with CGP in China

At the end of last year, Telix Pharmaceuticals announced a major deal with China Grand Pharmaceutical and Healthcare Holdings (CGP) which is the same group that acquired Sirtex Medical in 2018. The deal came with a US$25 million upfront payment, a US$25 million investment, milestone payments of up to US$200 million, and royalties from sales.

Through the deal CGP has gained access to Telix's molecular-targeted radiation products for the regions of China, Hong Kong, Macau and Taiwan. The deal was also an important validation of Telix's business model.

Since listing in 2017, Telix has become a billion-dollar business (by market capitalisation) in just three years, boasting the record of the fastest Australian biotech to reach this status (see table below).

Billion Dollar Biotech Race

Company	Time from listing or tech acquisition to reach $1 billion market cap
Telix Pharmaceuticals	3 years
Mesoblast	6 years
Imugene	7 years 5 months
Nanosonics	9 years 4 months
Polynovo	11 years
Clinuvel Pharmaceuticals	17 years 7 months

4.Cogstate - Signed US$45 Million Licensing Deal with Eisai

In a transformative deal for Cogstate, last year the company licensed global rights to its computerised cognitive tests, outside of clinical trials, to Japanese pharmaceutical group Eisai Co. Ltd. Cogstate received US$15 million up front and will receive at least US$30 million from minimal sales royalties.

The latter has since become guaranteed following the approval of the world's first disease-modifying Alzheimer's disease drug, Aduhelm. Eisai and Biogen are co-marketing the drug, with Eisai set to launch Cogstate's test in the US shortly. The test is also expected to be launched in Europe in two years and in China in three years time. The Cogstate test will (presumably) help Eisai screen for patients with cognitive decline who may be suitable for Aduhelm treatment.

Since the decision by Eisai and Biogen was made to resurrect the plaque busting drug Aduhelm in 2019, Cogstate's business prospects have soared. Cogstate's core business is from use of its cognitive computerised test in Alzheimer's trials. This week the company announced it had signed US$38 million of new contracts in just the last two months.

5.Ellume (private company) Sells US$232 Million of Corona virus Tests to US Government

In February this year, diagnostic company Ellume inked a deal with the US Government to supply its at-home SARS-CoV-2 test worth US$232 million. Its self-user test has an accuracy of 96%. This followed a separate US$30 million grant last year from the NIH in the US. The company was expecting to increase its employee count at its Brisbane facility from 350 to 500 people and intends to build a US facility that will employ around 1,000 staff.

6.Mesoblast - Receives CRL from FDA, Raises $351 Million

In October last year stem cell leader Mesoblast received a Complete Response Letter (CRL) from the FDA, which meant the company would not receive marketing approval at that time, for its stem cell treatment for graft-versus-host disease in children. This was despite an FDA advisory panel voting 9:1 in favour of the drug in August.

The FDA requested that the company complete at least one additional study. The regulator requested additional rational to show the relationship between potency and biological effect. The company will need to address potency assays for its product.

An issue with stem cell treatments is their potency and reproducibility between batches as the original master stem cell bank continues to divide and generate new stem cells.

Last year Mesoblast also signed a global collaboration deal with Novartis for its remestemcel-L therapy for acute respiratory distress syndrome, including from COVID-19. Novartis will also have an option to become the commercial distributor for the therapy for GvHD outside of Japan. The license remains subject to some closing conditions relating to the COVID-19 ARDS trial.

7. Imugene - The Most Recent Billion Dollar Biotech Raises $90 Million

Last financial year cancer immunotherapy company Imugene experienced a 10-fold increase in its share price to become the newest billion-dollar biotech on the ASX. The company recently raised $90 million in a transformational capital raise to fund its suite of novel immuno-oncology therapies. Imugene is now capitalised at $1.7 billion.

Imugene is another success story from biotech entrepreneur Paul Hopper, who was previously involved with Viralytics, which was sold to MSD for $502 million, and recently listed the CAR T technology company, Chimerix Therapeutics on the ASX. Hopper is also executive chairman of Radiopharm Theranostics, which recently raised $20 million. The company is still private at this stage.

8. Planet Innovation - Business Surges Alongside Industry Demand

Planet Innovation is a private company based in Melbourne that services the biotech industry with product design and manufacture. It has an emphasis on assisting companies with the development of diagnostics. In the first half of FY2021 the company

increased revenue by 139% to $66 million. It also added 100 staff in the period with sights on an IPO.

The company has three arms. One is the provision of engineering design services. The second is in product manufacture for those same companies once products are approved. And the third is its venture business, where it invests in start-ups and spins them out of the business as they mature. One of those companies, Lumos Diagnostics, recently listed on the ASX.

9. Immutep - LAG3 Pathway Validated, Raises $60 Million

Immutep is developing immunotherapeutic drug candidates for the treatment of cancer and autoimmune diseases. Its key platform is around the LAG-3 pathway with the LAG-s gene discovered by Immutep's CSO Frederic Triebel.

Over the last year validation of the LAG-3 pathway has occurred from Bristol Myers Squibb with its LAG-3 inhibitor relatlimab. In a major Phase II/III study (in 714 patients with advanced melanoma), the LAG-3 inhibitor showed a 5.5 month progression-free survival benefit (in combination with Opdivo compared to Opdivo alone). LAG-3 is becoming an increasingly more active area for pharmaceutical companies. The president of Merck Research Laboratories said recently that LAG3 inhibitors, CTLA4 inhibitors, TIGIT inhibitors and ILT4 inhibitors can all be added to PD1 drugs, such as Keytruda, to improve their baseline activity.

Immutep has four internal trials underway with a LAG-3 agonist. There are four Phase II trials underway by Novartis with a LAG3 inhibitor licensed from Immutep. And GlaxoSmithKline currently has a LAG3 depleting antibody in a Phase II study.

Results in the last year with Immutep's Phase II study in second line head and neck cancer (HNSCC) treatment showed an overall response rate of 46% (in patients with PDL1 levels of at least 1%) compared to a response rate historically of 17% for Keytruda alone. Of interest is that three of the responders in the trial of 37 patients had PDL1 levels of less than 5%, when generally Keytruda alone does not work well.

MSD and Immutep are now conducting a 160-patient study in first line patients with the combination therapy.

10. Micro-X - Ready for Take Off

X-ray technology company Micro-X has had a very eventful two-year period. Demand for its lightweight x-ray systems grew significantly over the last year as a result of the pandemic and the need to x-ray suspected COVID-19 patients for pneumonia.

Whilst this surprise additional demand has been an opportunity for the company's instrument to gain a foothold in the global x-ray machine market, it's been a period of significant business restructure and technology advances.

During the period, the company has installed in-house capacity to make all the major components of its lightweight x-ray machines. Most important is the production of carbon nanotube emitters, which were brought in house in 2019, and more recently the capability to make the high voltage generators.

The company's distribution deal with Carestream for its first instrument was moved to non-exclusive, which means the company is now selling direct and able to appoint regional distributors. Micro-X recently appointed Roesys to distribute the Rover x-ray instrument in Europe, Africa and the Middle East. The Rover instrument has been approved in the US under the Micro-X brand (previously approved through Carestream).

Other restructuring in the last two years included cancelling of a major collaboration with the transportation and aerospace group Thales AVS France SAS, due to that group's impact from the pandemic. This has allowed Micro-X to complete development of the Mobile Backscatter Imager (now called the IED X-ray Camera) in house.

The major driver for the company in the next 12 months will be sales of the IED X-ray Camera to bomb disposal units. This device will not require regulatory approval, should receive strong and immediate demand, and will sell for around US$350,000 each (by our estimates).

The company has also secured two initial contracts with the Department of Homeland Security (US$4 million) to design the next level of airport check-in security systems that will incorporate Micro-X's imaging systems.

And importantly the company secured $34 million in additional funds earlier this year through a placement and SPP that should fund the business until significant sales are generated from its products next year. The company generated cash receipts of $5.3 million last financial year.

Bioshares

Dimerix Funds PHASE III FSGS Study with $20 Million Raise

Dimerix (DXB: $0.315) has announced a substantial and important capital raise that will help fund the company's Phase III program in FSGS (focal segmental Glomerulosclerosis). A total of $20 million will be raised at $0.20 per share with Merchant Fund Management being a cornerstone investor in the raise.

Up to a further $2 million will be raised through an Share Purchase Plan (SPP) to smaller shareholders. The company's limited funding to date has been a restriction for the company's commercial development plans with news of the capital raise surging the company's share price 58% above the offer price for the new share issues.

The Phase III study will seek to recruit between 120 - 180 patients with the orphan kidney disease FSGS. The first part of the study, in 68 patients, is expected to start dosing patients this year with interim results from those patients at the end of next year.

The trial and capital raise is structured such that investors will receive one option for every two shares subscribed for, with that option having an exercise price of $0.40. The options expire in July 2024. However, that expiry date is brought forward to one month after the interim results (from the 68 patients) if an independent committee recommends the trial continues. This means the second part of the study is then funded from exercising of the options, which should raise an additional $20 million (assuming a share price in excess of $0.40).

In the first part of the study (in 68 patients) the participants will be treated for 26 weeks. Those patients will then move into the second part of the study (pending an independent decision to continue based on interim results) in which 120-180 patients will be treated for 35 weeks. The treatment will be Dimerix's drug candidate DXB-200 plus an angiotensin receptor blocker (ARB), such as irbesartan, and compared to treatment with an ARB alone. (The final study design is still to be confirmed with the FDA.) The trial will be conducted across 68 sites in the US, Europe, Australia and Asia.

After the 35 weeks of treatment, and depending on the clarity of results, Dimerix may file for accelerated approval using the endpoint proteinurea. Final results will be after an additional 52 weeks where the endpoint will be eGFR (glomerular filtration rate through the kidneys) for which standard FDA approval may be sought.

Phase II Results

In a Phase IIa crossover study, where all patients received both the placebo and DMX-200 with a six week break in between, 89% of patients taking DMX-200 achieved a reduction in proteinurea levels compared to placebo. (All patients were on ARB (irbesartan) therapy as well). Whilst the results were clearly positive, it was a small study with 10 patients and seven who were evaluable for final analysis.

Well Structured Funding

The well-structured trial and capital raise is an innovative way to fund the Phase III study in stages with interim independent reviews. FSGS is more than a billion-dollar market opportunity according to the company. There are no current therapies with kidney failure occurring five years from diagnosis. Only one Phase III study is required, with the potential for early US approval under an accelerated approval process. Dimerix should also be entitled to an R&D tax rebate for the trial with the majority of the program work so far having been conducted in Australia.

COVID-19 Studies

Dimerix's lead drug candidate, DMX-200, which is a CCR2 antagonist, is currently being assessed to two global Phase III studies for the treatment of COVID-19. Both studies, the REMAP-CAP (in around 200 patients treated with DMX-200 and 7,000 patients in total investigating multiple therapies) and CLARITY 2.0 (in around 600 patients in India) are expected to complete recruitment this year with results early next year.

In the REMAP-CAP study the patients are assessed out to 21 days and for CLARITY 2.0 patients are treated out to 14 days, with both studies comparing treatment with DMX-200 against standard-of-care, with the CLARITY 2.0 study also including ARB therapy.

The rational for trialling DMX-200 in COVID-19 patients is that DMX-200 is an anti-inflammatory that blocks the CCR2 receptor. In a paper published last year, authors looked at pro-inflammatory cytokines in the lung that can cause a cytokine storm, which result in severe respiratory disease in 5%-10% of people infected with SARS-Co-V-2. The authors concluded that **"Targeting airway-derived cytokines such as CCL2 through CCR2 antagonists or other airway-specific mediators may be more effective in reducing lung damage or even promoting recovery from ARDS in severe COVID-19".** *(Szabo et al.…Analysis of respiratory and systemic immune responses in COVID-19 reveals mechanisms of disease progression.)*

Dimerix CEO Nina Webster said that DMX-200 is the only CCR2 antagonist in clinical development.

Summary

Dimerix is now well funded to conduct a global PHASE III study in FSGS that represents a billion-dollar market opportunity. Only one Phase III trial may be required to gain accelerated approval. Plus other opportunities for DMX exist in the treatment of diabetic kidney disease and in limiting the long term lung damage caused by the cytokine storm in serious COVID-19 infections.

Dimerix is capitalised at $97 million (after completion of the capital raises).

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

ResApp Health Signs Licensing Deals for Europe, the Philippines and Indonesia

Digital health company ResApp Health (RAP: $0.048) has signed licensing deals with Medgate and Alodokter, which will incorporate ResApp's respiratory diagnostic aid, for use via smartphone.

Medgate, which is Europe's largest telemedicine provider, has undertaken a six-month trial with the ResAppDx product. The product uses cough signatures recorded through a phone and analysed with proprietary software to help diagnose multiple respiratory infections and conditions.

It has been well received by patients and doctors according to ResApp CEO Tony Keating, with accuracy rates similar to that achieved in clinical studies (above 80%). Keating said the company's test helped detect some cases that would have been missed by the doctors.

Medgate has around 200 doctors who provide its telehealth service in Switzerland, now Germany and in the Philippines. One restriction with the test is that it is used through the Medgate app, which requires patients to log into that system. However, ResAppDx is not used in telephone-based consultations at this point with Medgate. ResApp is in discussions with Medgate to make its test used outside of the Medgate app, whereby patients are sent an SMS, cough into the phone, and the results are delivered to the doctor. Keating is seeking to make the facility available through Medgate in the next six to 12 months.

ResApp has also signed a license agreement with Alodokter in Indonesia with the ResAppDx test expected to be used on their telemedicine platform at the end of this year. This was without any pilot program being undertaken. The pricing for telemedicine is lower in Indonesia although it is a substantially larger patient population.

At this point both licensing deals are not expected to have a 'material impact on operating results' with the emphasis on the company being able to gain widespread global adoption. Keating said that the company has between five to 10 discussions underway with other telemedicine providers, with some of those at the contract negotiation stage.

ResApp has also partnered with Ilara Health in Kenya to distribute the ResAppDx test into healthcare clinics. ResApp is paid per test with clinics now utilising the product.

ResApp Test for COVID-19 Disease Assessment and Management

ResApp is now conducting two trials, one in the US (previously announced) and one in India that are looking to both help screen patients for COVID-19 using a cough-based algorithm, to help triage patients (i.e. those with mild COVID-19 to remain at home and those with progressive disease to receive emergency hospital care), and to look at the long term effects of COVID-19 on patients.

Rapid recruitment is expected in the Indian study of 100 COVID-19 positive patients who will also be followed to deliver longitudinal data. With the coronavirus looking to be a long-term global concern, tools for better diagnosis and disease management will continue to be sought after.

ResApp is capitalised at $40 million with $6.6 million in cash at June 30.

Bioshares recommendation: Speculative Buy Class B

Bioshares

Patrys Incurs Six Month Delay as Opportunities Continue to Expand for its Cell Penetrating Technology

Patrys (PAB: $0.036) has received a six-month setback in its clinical trial program due to supply delays caused by the coronavirus pandemic. The first clinical study with the company's lead drug candidate PAT-DX1 is now expected to start in 2H 2022 (previously 1H 2022).

The delay is due to the supply of the cell media that is required to manufacture the company's antibody. The antibody will now be made in Q4 this year, with the final step before clinical trials, toxicology studies, to be conducted in Q1 next year.

However, in the meantime there is a large amount of work going on around the world looking at the unique biology of Patrys' deoxymabs and how they can be harnessed to provide new therapeutic options for cancer patients. James Campbell, CEO, expects this work will lead to multiple publications on Patrys' unique deoxymab technology platform with up to six additional scientific papers to be published within the next 12 months.

The utility of the cell penetrating technology and its potential therapeutic benefit in oncology continues to expand. Patrys has reported preclinical data on PAT-DX1 in treating glioblastoma and metastatic triple negative breast cancer (TNBC). Last month the company released additional data showing that the drug candidate is also effective and slows tumour growth in an animal model of pancreatic cancer by 26% and this resulted in a 47% improvment in median survival in mice.

This is the third difficult-to-treat tumour type in which PAT-DX1 has shown promising efficacy in (albeit in mouse models). Around 15-20% of pancreatic tumours have DNA damage repair mutations, which is where PAT-DX1 has the potential to be effective as a single agent therapy. Similarly around one fifth of triple negative breast cancer (TNBC) tumours have DDR mutations, and in glioblastoma, around 35% of tumours have the PTEN mutation that would potentially make PAT-DX1 an effective oncology treatment as a single agent.

One of the appealing features of PAT-DX1 is that it can make its way into the cancer cell nucleus and interfere with the DNA damage repair process. When targeted against a tumour that already has an impaired DNA damage repair system, it is believed the combined effect PAT-DX1 has on blocking DNA damage repair results in an amplified impact in preventing tumour growth and enhancing survival. Consequently, PAT-DX1 can be used as a single agent in tumours that already have impaired DNA damage repair processes, or in combination with other oncology drugs or radiation that cause damage to DNA and increase the repair burden within the cancer cells.

It has also been shown in a mouse model to that PAT-DX1 is able to cross the blood-brain-barrier. This opens up the possibility of using PAT-DX1 as an effective therapy for brain cancers. To date few drugs and no antibodies are able to cross the BBB according to Campbell.

Recently Patrys added a second antibody to its pipeline, PAT-DX3, which can also cross the blood-brain barrier in a mouse model of primary brain cancer. Unlike PAT-DX1, which is a small antibody fragment, PAT-DX3 is a full-sized IgG antibody. The larger size of PAT-DX3 means it may be provide a better option for use as a targeting agent as an antibody drug conjugate (ADC) designed to transport other oncology drugs into the brain. Only 1.5% of current drugs can cross the blood-brain-barrier. Campbell said that the advantage of the full-sized antibody is that it offers more binding sites to attach payloads/drugs, compared to PAT-DX1.

Patrys has indicated that it is exploring opportunities for developing antibody drug conjugates (ADCs) using its deoxymab platform, and believes that the tumor-seeking attributes of both PAT-DX1 and PAT-DX3 make them especially well-suited for developing ADCs for cancers where there are no existing targeting antibodies.

Summary

The applications for Patrys' unique antibodies for the treatment of solid tumours can be expected to increase as the company proceeds to its first clinical studies in 2H 2022.

The Phase I study is expected to recruit 12 patients with various solid tumours, particularly with tumour mutations that already have impaired DNA damage repair systems.

Patrys is capitalised at $69 million.

Bioshares recommendation: **Speculative Buy Class B**

A comparison between Patrys and PYC Therapeutics is provided on the following page.

Bioshares

Side-by-Side

A Comparison of Cell Penetrating Technology Companies: PYC Therapeutics v Patrys

Two ASX listed companies that can be compared are PYC Therapeutics (PYC: $0.145) and Patrys (PAB: $0.036). Both are at the pre-clinical stage of development, both are seeking to commercialise unique technologies that have cell penetrating capabilities, and both companies are seeking to move into clinical trials in 2H CY2022.

PYC (formerly Phylogica) was built on the platform of abundant peptide libraries that it had developed internally. From that library it found a family of peptides with cell penetrating capabilities.

The company is now working on using the technology to deliver RNA therapeutics (antisense) into cells concentrating on eye diseases. To achieve this it has hired Professor Sue Fletcher who was a co-inventor of the antisense therapy Exondys-51 from Sarepta. The company has shown that it can induce exon skipping in diseased human cells in *in vitro* studies.

The aim for PYC is to build an RNA therapeutics company using its cell penetrating peptides led by the expertise of Professor Fletcher. The market for its lead indication, in retinitis pigmentosa type 11, is estimated at over $1 billion a year.

Continued over

Comparison: PYC Therapeutics v Patrys

	PYC		PAB
Share price	$0.15		$0.036
Market Cap	$477M		$66M
Cash	$51M		$10.9M
R&D expenditure	$11.6M		$2.7M
Net cash outflow FY2021	$12M		$3.9M
Source of original research, current collaborators, researchers	Lions Eye Institute (Perth), CSO Prof Sue Fletcher (Co-inventor of Exondys-51 from Sarepta)		Yale University
Preclinical data	Shown CPP* can deliver antisense payload into human cells (in vitro), achieve exon skipping and treat retinal disease. Exon skipping achieved in mice retina using CPP as delivery of RNA		Positive results in mouse model of glioblastoma, TNBC and pancreatic cancer, and shows to cross BBB in mouse studies
Drug candidates cross blood-brain barrier	No		Yes
Stage of development	In vivo ocular PK distribution and tox studies underway		Stable high yield cell line developed. Engineering run of GMP material to be completed CY2021.
Clinical studies	IND to be filed mid 2022		To start 2H CY2022
Target diseases	Retinal diseases, CNS disorders		Solid tumours
Technology	Cell penetrating peptide for RNA delivery		Cell penetrating antibody, deoxymab, derived technology platform (derived from animal model of human lupus)
Lead candidates	VP-001 (retinitis pigmentosa type 11) VP-002 (autosomal dominant optic atrophy)		PAT-DX1 (dimer of binding domains of deoxymab,humanised form). PAT-DX3 humanised form of deoxymab, full IgG antibody
Mode of action	RNA enters cells with proprietary CPPs		Enters cancer cell nucleus and interrupts DNA repair process
Capacity for conjugation with other drugs to bring into cells?	Yes		Yes
Recommendation:	**Switch to PAB**		**Speculative Buy Class B**

**CPP - Cell penetrating peptides*

Bioshares Model Portfolio (25 August 2021)

Company	Code	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Clinuvel Pharmaceuticals	CUV	$28.35	$20.31	Hold	$1,401	November 2020
Opthea	OPT	$1.410	$0.160	Spec Buy A	$490	November 2014
Immutep	IMM	$0.475	$0.320	Spec Buy A	$404	March 2019
Cogstate	CGS	$1.715	$0.24	Buy	$293	April 2019
Micro-X	MX1	$0.255	$0.38	Spec Buy A	$117	May 2017
Dimerix	DXB	$0.315	$0.09	Spec Buy A	$97	December 2018
Cynata Therapeutics	CYP	$0.520	$0.70	Spec Buy B	$75	December 2020
Patrys	PAB	$0.036	$0.013	Spec Buy B	$65	July 2020
Pharmaxis	PXS	$0.110	$0.260	Spec Buy B	$50	December 2016
LBT Innovations	LBT	$0.125	$0.08	Spec Buy B	$36	May 2021
Acrux	ACR	$0.120	$0.31	Spec Buy A	$34	July 2017

Portfolio Changes

IN:
No changes

OUT:
No changes

Stocks Removed from Bioshares Portfolio in TTM

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

Following on from retinal diseases, PYC will also be targeting CNS diseases with the same technology, however it still needs to address the delivery issue into the brain/CNS.

Over the next year key milestones for PYC will be data from rabbits and primates prior to launching a clinical study in retinitis pigmentosa with its lead candidate VP-001. Its second candidate, VP-002, for the treatment of autosomal dominant optic atrophy, is around six months behind the first program according to the company.

PYC is well funded with $51 million in cash. It is seeking a future US IPO to build its cash base even further. Patrys had $11.6 million in cash and is funded to get through its first clinical readout. PYC management is based in California with research out of Perth, while Patrys is based in Melbourne.

Both companies are at similar stages of development and expect to enter the clinic around the same time. An advantage of the Patrys antibody technology is its ability to cross the blood-brain-barrier. The two companies are seeking to leverage their technologies in different directions: Patrys has a focus on oncology, both as a monotherapy or in a conjugated form with other oncology drugs – to take drugs into cancer cells and into the brain; PYC is using its cell penetrating peptides to deliver antisense drugs for a variety of indications, initially in the ophthalmology space.

On a capitalisation basis, we view Patrys as the preferred investment option.

Bioshares recommendation (PAB): **Speculative Buy Class B**
Bioshares recommendation (PYC): **Switch to PAB**

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

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