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Companies covered: **ADR, MEB, PXS, Cash Flow Analysis**

	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%
Cumulative Gain	699%
Av. Annual gain (14 yrs)	17.1%

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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

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Bioshares

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

Extract from Bioshares –

Pharmaxis – A Drug Developer with a Deal Making Record

Pharmaxis (PXS: $0.315) has reported its results for Q3 FY2018. The company generated sales of $1.7 million with a net profit for the quarter of $8.1 million following the receipt of a $15.2 milestone payment from Boehringer Ingelheim in January. The company finished the quarter with $34.5 million in cash.

Pharmaxis has received two milestone payments from Boehringer in the last 12 months. One for $27 million when the first patient started treatment for NASH with the drug candidate created by Pharmaxis, and $15.2 million when the first patient was treated with the same drug candidate for diabetic retinopathy.

The next milestone payments are due when these programs move into Phase III studies, with €62 million due, and then a further €300 million due on filing for approval, marketing clearance and pricing approvals.

Both of these current Phase IIa studies are expected to be completed in around 12 months time (1H 2019). Patients in both studies will be treated on drug for three months.

The efficacy outcome for the diabetic retinopathy study has been set substantially higher, with Boehringer seeking to achieve a two line improvement in vision following daily oral treatment with the anti-inflammatory drug candidate acquired from Pharmaxis (an SSAO inhibitor). This is a clinical proof-of-concept study and will likely move quickly into a Phase IIb study if the primary endpoint is achieved.

The NASH study will require longer term data to show clinical evidence of improvement in disease. The results in the NASH study will be more around evidence of target engagement and selection of the optimum dose for the Phase IIb study that is expected to follow, pending positive Phase IIa results. Secondary endpoints in the NASH study will be early data around changes in liver function.

The reason Boehringer is investigating the compound in this second indication is that preclinical work conducted by Boehringer shows that the SSAO enzyme is strongly upregulated in diabetic retinopathy with higher SSAO levels directly correlated with disease severity.

About one third of patients with diabetes develop diabetic retinopathy, according to Pharmaxis CEO Gary Phillips, with one third of those patients going blind.

LOXL2 Program

The next program in development for Pharmaxis is the LOXL2 program. Pharmaxis has developed two anti-fibrotic drug candidates that inhibit the LOXL2 (and LOXL3) enzyme. There are many different applications so Pharmaxis is running two drug candidates against this target in Phase I studies.

Continued over

Phase I single ascending dose studies have been completed. It shows that the compounds inhibit the LOXL2 target using a assay developed by Pharmaxis. This is from a single oral dose which shows effectiveness in a dose dependent manner. This is a positive achievement over competitors such as Gilead that failed to show target engagement in Phase I studies with its LOXL2 inhibitor.

The next stage is a multiple ascending dose, whereby volunteers receive daily doses of the drug treatment for 14 days.

In combination with these Phase I studies, Pharmaxis is conducting three month toxicology studies. This is an important addition as it will allow a potential partner to move directly into a Phase II program after securing a licensing deal with Pharmaxis.

The two compounds that have moved into Phase I have different pharmacokinetic profiles with take up in different parts of the body, one being preferentially taken up by the liver. Success with multiple compounds for Pharmaxis will also help build the data package for partnering believes Phillips.

Pan LOX program

The second in-house program in development by Pharmaxis is against the LOX family of enzymes. There are five enzymes - LOX, LOXl1, LOXL2, LOXL3 and LOXL4. LOX and LOXL2 are associated with fibrosis in the skin.

A topical drug against these targets could be used to reduce scarring for wounds such as burns. The LOX enzymes are implicated in diseases such as myelofibrosis and pancreatic cancer. Blocking this entire family of enzymes could provide a useful short-term treatment for such diseases.

Pharmaxis is seeking to move this program into Phase I studies early in 2019. Preliminary animal data is positive.

MPO

A second preclinical program is expected to enter the clinic also in early 2019, which will be a compound that inhibits both the SSAO enzyme (which the Boehringer compound targets) as well as the myeloperoxidase enzyme (MPO).

Pfizer had a MPO inhibitor targeting NASH in Phase I which it axed in January this year. AstraZeneca previously had an MPO inhibitor in clinical studies for the treatment of Parkinson's disease but has no clinical studies underway currently.

Pharmaxis will be developing this program as a potential treatment for inflammatory bowel disease, and respiratory and cardiovascular diseases.

Bronchitol for Cystic Fibrosis in the US

Pharmaxis' partner for Bronchitol, Chiesi Farmaceutici, in the US (and the UK, Germany, Ireland and Italy most recently) is expected to file this drug for approval towards the end of this year.

The third Phase III trial, conducted in the US, was completed in July last year. The reason for the delay in filing is because of changes to the way inhaled drug applications are assessed by the FDA (now as combination therapies) and the need to reorganise the data from the Phase III studies. Upon commercial launch, Pharmaxis will receive a US$10 million payment from Chiesi.

Results from the US study showed that lung function was increased by only 2.2% (compared to an average 7.3% in the first two studies) although the results were statistically significant.

Bronchitol (and Aridol) sales progress

We do not consider the Bronchitol and Aridol products as core to the Pharmaxis business. However, this business unit looks to be moving closer to being profitable.

In the last quarter, the loss (EBITDA) was $1.1 million. The loss for the full year is expected to be around $3.7 million, compared to a loss for FY2017 of $7.1 million. The business is expected to break even over the next 18 months.

Sales to Western Europe (UK, Ireland, Germany, Italy, Australia, Denmark, Sweden and Spain) were $0.93 million, up from $0.59 million in the previous quarter. However, this quarter included sales to Chiesi, which occur around every six months.

Sales in Australia increased to $0.29 million from $0.22 million the previous quarter due to improved reimbursement in Australia from January 1, 2018. Patients in Australia can now take Bronchitol and Pulmozyme and be reimbursed for both drugs.

In Russia, Bronchitol has been sold previously although sales are lumpy. Several hundred patients in Russia have gained access to the drug, which is currently a $29 million market. Pharmaxis is seeking reimbursement to the remaining 4,000 patients with CF in Russia. The next sale to Russia is expected later this year.

Summary

In a quarterly update to shareholders, Pharmaxis' CEO noted that the acquisition by Merck of Viralytics (as announced in February) exposed a large gulf between the on-market valuation of Australian biotechs and the price large pharmaceutical companies are willing to pay.

While this ‘gulf’ may not apply across the board, and noting that financing risk is a significant factor in this discrepancy for some companies, Pharmaxis continues to represent a substantially discounted investment opportunity.

The company is capitalised at $101 million and retains a technology valuation (capitalisation minus cash) of only $67 million.

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 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,Viralytics, Opthea, RHS, ResApp, Pharmaxis, Dimerix, Cyclopharm, Adalta, Medibio, Phylogica, Pharmaust