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Companies covered: **CYC, PXS, VHT**

	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 - Current)	73.6%
Cumulative Gain	1255%
Av. Annual gain (19 yrs)	19.1%

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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[at}bioshares.com.au

David Blake - Editor/Analyst
Ph: (03) 9326 5382
Email: david[at]bioshares.com.au

Mark Pachacz - Editor/Analyst
Ph: 0403 850 425
Email: mark[at]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*

PXS Completes Phase Ia Trial of PXS5505A

Pharmaxis (PXS:$0.21) has completed the Phase Ia component of its Phase I study program for an oral pan-LOX inhibitor, PXS-5505A. This drug candidate targets all members of the lysyl oxidase family members (LOX, LOXL1, 2,3 and 4), which are implicated in fibrosis.

PXS-5505A is being developed to treat myelofibrosis and pancreatic cancers.

In pancreatic cancer, fibrotic stroma (connective tissue) form to create barriers which many anti-cancer drugs have difficulty passing. The LOX family of enzymes are potential targets because of the role they play in promoting collagen cross linking (which results in hardened or fibrotic tissue). Inhibiting such cross linking could destabilise the fibrotic stroma and enable other drugs to gain more traction in attacking the tumour.

LOX has been found to be a regulator of bone marrow fibrosis in mouse models of myelofibrosis and upregulated in human myelofibrosis cells and plasma. (see Leiva O et al, "The role of the extracellular matrix in primary myelofibrosis", *Blood Cancer Journal*, Feb 2017)

The Phase Ia study evaluated four doses of PXS-5505A, ranging from 50mg to 300mg, along with a placebo. The higher doses of 200mg and 300mg were found to have the most inhibitory effect. Forty healthy subjects were dosed in the trial, with each subject being given a single dose. The drug was found to be well tolerated.

The Phase Ib component of the trial, which commenced on October 15, will evaluate multiple ascending doses of PXS-5505A in 16 healthy subjects over 14 days. Results are expected in H1 2020.

The company has also now successfully completed three-month toxicology testing of PXS-5505A.

Looking ahead, events to monitor include the results of partnering discussions for Pharmaxis' LOXL2 inhibitors (two compounds, PXS-5382A and PXS-5338K), along with the release of results for Boehringer Ingelheim's Phase IIa trial of BI 1467335 (formerly PXS-4728A) in NASH.

The double blind, randomised, placebo controlled Phase II trial of BI 1467335 enrolled 114 patients with clinical evidence of NASH and evaluated four doses of drug given once daily, over 12 weeks.

Pharmaxis is capitalised at $83 million and held cash of $31 million at June 30, 2019. The company received a tax refund of $6.2 million earlier this month.

Bioshares recommendation: **Speculative Buy Class A**

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Some Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Cogstate, Bionomics, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Emvision, Antisense Therapeutics, Heramed, Imugene, Exopharm, Immutep, Neuroscientific Biopharmaceuticals