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Companies covered: **IMM, PXS, RAP, ZLD**

	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)	73.3%
Cumulative Gain	1253%
Av. Annual gain (19 yrs)	19.1%

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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 Remains Confident of Securing LOXL2 Deal

Pharmaxis' (PXS: $0.11) share price has fallen by 52% since December 18, 2019, when Boehringer Ingelheim decided to stop its NASH drug development program with a compound bought from Pharmaxis. That share price decline can also be attributed to a licensing deal for the company's LOXL2 program taking longer than expected to finalise. However, the company continues to progress licensing discussions for this program, and if secured, should see an immediate response in its share price.

The main reason a licensing deal is taking longer than expected is due to concerns about a rival company's failure with a different compound seeking to engage the same target that Pharmaxis is seeking to block, that being the LOXL2 enzyme.

However, Pharmaxis CEO Gary Phillips believes that the LOXL2 inhibitors developed by Pharmaxis are far superior to the antibody, simtuzumab, that was tested and failed in five clinical studies by US biotech Gilead Sciences.

One of the main issues with the Gilead program, which was acknowledged by that company, was that it progressed the program without any evidence of target inhibition from a human pharmacokinetic or human pharmacodynamic assay.

In contrast, Pharmaxis has developed *in vitro* assays, both pharmacokinetic and pharmacodynamic, to confirm target inhibition. It has also confirmed target inhibition in animal models and in Phase I human studies.

As a direct comparison, the Gilead compound was able to achieve only 40%-50% inhibition of the LOXL2 enzyme, compared to over 90% target inhibition with the Pharmaxis compounds within 24 hours. Being an antibody, and larger than a small molecule, simtuzumab may well have had poor mobility to the target sites as well according to Phillips.

The Pharmaxis compounds also inhibit the LOXL3 enzyme, for which the Gilead compound showed no inhibition.

Continued over

A by-product of the failed Gilead programs with simtuzumab is that a licensing deal for Pharmaxis may be structured initially as an option deal, rather than a product acquisition deal as seen with the Boehringer transaction.

This may involve Pharmaxis conducting a proof-of-concept Phase II study that could be funded by a potential partner. If a deal is structured with an option agreement, the total deal value will likely be worth more for Pharmaxis.

Other Milestones for 2020

Although one program has been shut down in the Pharmaxis pipeline, that being in NASH by Boehringer, Pharmaxis has multiple programs that are progressing through the clinic.

These include:

- The LOXL2 program which is ready for Phase II assessment and partnering
- A Phase IIa study in diabetic retinopathy (conducted by Boehringer Ingelheim) with results in H2
- A Phase II systemic LOX inhibition study in myelofibrosis (H2), with inhibition of LOX, LOXL1, LOXL2, LOXL3 and the LOXL4 enzymes involved in severe fibrotic conditions
- A Phase I topical LOX inhibition study in scar treatment (H2), and
- US FDA approval of Bronchitol for the treatment of cystic fibrosis in the US (H2) which will include a US$10 million milestone payment to Pharmaxis from Chiesi Farmaceutici

Pharmaxis is capitalised at $43 million and finished last year with $26 million in cash.

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

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