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BIOSHARES
Australia's Independent Biotech Investment Resource, est.1999

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	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 - May '22)	-15.6%
Year 22 (May '22 - Dec '22)	-2.2%
Year 23 (CY2023)	-19.9%
Cumulative Gain	1245%
Av. Annual gain (22 yrs)	18.1%

Companies covered: **DXB, HIQ, IMU, MSB, MX1, PXS, RSH, TLX**

2023 Top Six Picks: -14.6%

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Extract from Bioshares –

Pharmaxis - Meaningful Impact on Bone Marrow in Myelofibrosis Study

Pharmaxis (PXS: $0.05) has released interim results from its Phase II study with PXS-5505 in patients with myelofibrosis. Results from the first 10 patients who completed six months of treatment are now available.

Myelofibrosis is characterised by fibrosis of the bone marrow, which leads to lower production of blood cells (red and white blood cells and platelets), and an increased spleen size, which attempts to make up for the deficiency by producing more blood cells.

The main treatment is with JAK inhibitors, however most patients come off treatment, according to Pharmaxis CEO Gary Phillips, at which point they have only around one year to live. Pharmaxis' Phase IIa study is in patients who have failed this therapy.

The Phase IIa study has been difficult to recruit patients, with the Pharmaxis study being conducted across 20 sites, with 21 patients enrolled, and 10 having ceased treatment due to lack of response or non-drug related adverse events.

One of the very important outcomes from the study has been that PXS-5505 has been very well tolerated, which is a very appealing feature given the side effects of the mainstay JAK inhibitor therapies. It means that PXS-5505 may well be suitable as a combination treatment with JAK inhibitors. Phillips said there are other drugs in development for myelofibrosis but nearly all have issues with tolerability.

On efficacy measures, seven of the 10 patients had either stable or improved haemoglobin levels after six months, and eight of the 10 patients had stable or improved platelet levels. Five of the nine evaluable patients had an improved bone marrow fibrosis score, potentially indicating a disease modifying treatment. Dr Lucia Masarova from the MD Anderson Cancer Center, who was the principal investigator of the study, said that the effect on bone marrow is 'particularly exciting' and unprecedented where there are still no antifibrotic drugs available for this disease.

Move into Combination Study

Pharmaxis will now extend the existing study into combination therapy with a JAK inhibitor at the existing 20 sites, with recruitment expected to start this year. Enrolment should be easier given the safety information now known on PXS-5505, the larger patient population who are on JAK inhibitor therapy, and that patients are healthier than those who have failed current therapies.

The FDA is currently reviewing the trial protocol, following a meeting last quarter with the regulator. Pharmaxis expects it will be able to move straight into combination therapy without a dose escalation phase with the combined therapy given the strong safety profile of PXS-5505.

The combination study will also be open label with data expected by the end of 2024, at

Continued over

which point the company will plan for a pivotal study. Phillips said that after a slow start, clinical development of PXS-5505 in myelofibrosis is now accelerating.

Commercial Value of PXS-5505

The market for JAK inhibitor drugs for myelofibrosis is in excess of US$1 billion a year. Phillips said that the last three companies that achieved positive Phase IIb data in myelofibrosis were able to achieve deals worth in excess of US$1.5 billion (see table for recent deals).

Pharmaxis finished June with $9.2 million in cash and $5.2 million is expected to be received from its R&D tax rebate. Pharmaxis is capitalised at just $36 million.

Bioshares recommendation: **Speculative Buy Class A**

Myelofibrosis Drug Development Deals

Date	Company	Acquiror	Value	Stage of development
June 2021	Constellation Pharmaceuticals	Morphosys	US$1.7 billion	Phase IIb data from combination study in 400 pts
April 2022	Sierra Oncology	GlaxoSmithkline	US$1.9 billion	Completed Phase III
November 2022	Imago Biosciences	Merck	US$1.35 billion	Phase IIb data in 89 pts
May 2023	CTI Biopharma Corp.	Sobi	US$1.7 billion	Approved

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, Opthea, Pharmaxis, Dimerix, Patrys, Antisense Therapeutics, Imugene, Chimeric Therapeutics, Neuren Pharmaceuticals, Aroa Biosurgery, Radiopharm Theranostics, Imricor Medical Systems, Anteris Technologies, Bio-Gene Technology, EBR Systems, Immuron, Respiri, Clinuvel Pharmaceuticals