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Companies covered: ALT, PXS, RCE, RNO

	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 - current)	17.5%
Cumulative Gain	551%
Av. Annual gain (14 yrs)	17.7%

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

Extract from *Bioshares* –

Pharmaxis – NASH Continues to Attract Major Drug Development Deals

Pharmaxis (PXS: \$0.245) continues to progress its amine oxidase chemistry platform assets.

Boehringer Ingelheim has announced that it intends to move the SSAO inhibitor it bought from Pharmaxis last year into a Phase II trial in Q1 2017. That will bring with it an approximate \$25 million milestone payment to Pharmaxis.

Synairgen from the UK, which in-licensed a LOXL2 inhibitor last year, has announced positive preclinical data using its proprietary BioBank platform.

Synairgen's BioBank uses human tissue samples of different diseases on which to conduct drug development work. In this case, it tested the Pharmaxis LOXL2 inhibitors using lung cells from patients with idiopathic pulmonary fibrosis (IPF), which is the indication Synairgen has licensed, where lung cilia cells are grown. Pharmaxis is free to explore other indications for its LOXL2 inhibitors, including NASH (early liver disease or non-alcoholic steatohepatitis) and kidney fibrosis.

In the preclinical trials conducted by Synairgen, the Pharmaxis inhibitors were shown to be able to reduce cross-linking of collagen fibres in the lung tissue and achieve ordered collagen fibres in the presence of the LOXL2 inhibitors. The aim is to develop a once-a-day oral treatment for IPF.

Formal preclinical testing is expected to start this quarter with a Phase I trial in IPF expected to commence in H1 2017. Synairgen will fund the preclinical and Phase I studies.

Pharmaxis also expects to start its own Phase I trials with its LOXL2 inhibitors in 2017 in NASH or other diseases. Potential partners will be able to look at the preclinical package under a CDA with around 12 companies already interested, according to Pharmaxis CEO Gary Phillips.

Pharmaxis and Synairgen may look to conduct early Phase I licensing deals, which is what Pharmaxis was able to achieve with its SSAO inhibitor last year with Boehringer in the NASH (and other diseases including COPD) space. In that deal, Pharmaxis received an upfront payment of \$39 million in a deal worth up to \$750 million for one Phase I drug asset PXS4728A.

More Major Early Stage NASH Seals by Gilead

This week Gilead Sciences secured another program in the NASH space. It acquired the Nimbus Apollo subsidiary of Nimbus Therapeutics for an upfront payment of US\$400 million, predominantly for its Phase I NASH treatment program.

Cont'd over

Nimbus Therapeutics stands to receive a further US\$800 million in development milestones. Nimbus has been developing acetyl-CoA carboxylase inhibitors to treat NASH. These class of drugs work by reducing lipid levels in the body and may have an application also in treating obesity, diabetes and other inflammatory diseases in addition to NASH.

This follows a deal in 2011 when Gilead bought NASH antibody drug candidate, simtuzumab, from Arresto Biosciences for US\$225 million. That program was only at a preclinical stage of development and since the acquisition, a number of trials with this antibody since the acquisition have been terminated. Gilead also acquired a Phase II NASH program from German drug developer Phenex Pharmaceuticals in a deal worth up to US\$470 million last year.

Pharmaxis is capitalised at \$78 million. The company had \$45.9 million in cash at the end of December.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Major Drug Development Deals for NASH (Nonalcoholic steatohepatitis)

Date	Drug Developer	Licensee	Stage of Development	Deal Terms
December 2010	Arresto Biosciences	Gilead Sciences	Preclinical	US\$225M plus milestones
January 2015	Phenex	Gilead Sciences	Phase II	US\$470M total deal for FXR program, no royalties
May 2015	Pharmaxis	Boehringer Ingelheim	Phase I	\$750M deal total deal, \$39M upfront
April 2016	Nimbus Apollo	Gilead Sciences	Phase I	US\$400M up front, plus up to US\$800M milestones

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

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