

Companies covered: PXS, OCC, OSP, VHT

	Bioshares Portfoli
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%
Year 18 (May '18 - current)	-4.3%
Cumulative Gain	665%
Av. Annual gain (17 yrs)	17.1%

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Bioshares

20 July 2018 Edition 753

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

Extract from Bioshares –

The Metters Interview

In June last year Dr Kathleen Metters joined the board of Pharmaxis (PXS: \$0.31) as a non-executive director. Metters worked with Merck for more than 20 years, before commencing a career as a consultant. She trained originally as a biochemist, then went on to lead all of Merck's basic research with a team of 3,000 staff before designing and establishing Merck's External R&D group to bring external innovation into Merck.

We recently interviewed Metters, asking what makes one small drug developer look more attractive than another, compared to Big Pharma?

Metters said that Big Pharma is looking at ways to reduce the number of expensive clinical failures, trying to break the cycle of increasing investment into R&D with declining success rates. "They are looking to external companies in order to achieve that," she said.

Metters said that Big Pharma is looking for companies with clinical proof-of-concept but (these assets) are rare, expensive and it's a very competitive space. So they are being forced to look at earlier stage programs. They are looking for evidence that there is a high probability that the mechanism will translate clinically. They are also looking for well characterised molecules, a small molecule or antibody, (for which) they can unambiguously test the hypothesis, said Metters. They are not looking for programs that have concerns that need to be managed through the clinical trial process.

Metters said Big Pharma is also looking for a data package that has biomarkers for the molecule and for the disease to maximise chances of success in the clinic. Other positive considerations are if the first clinical trial indication can be completed in a short period, and pharma is looking for a company with a collaborative mindset.

What is driving the interest of Big Pharma in 'hot disease' areas such as NASH?

Metters said that one of the drivers (of interest) is breakthroughs in foundational science. "We have a deeper understanding of mechanisms that may be acting within a particular pathophysiology." These breakthroughs may have come through genomics or other routes. Often there a several discoveries that start to build out a field. Big Pharma is also becoming adept at breaking down a disease into smaller subsets of patients. NASH is a good example where there are different drivers to different types of liver disease.

Big Pharma now better understands the value of patient selection and the biomarkers and hallmarks of disease within different patient segments. This has also been driven by the costs involved in doing trials across large patient groups, so pharma is focusing more of patient sub-segments. "That's driven NASH to a degree," said Metters.

Metters said it is important to understand what is attractive to Big Pharma at any particular time. "Things go in and out of focus with Pharma," she said. Competitive viability and understanding what Pharma is looking for can change.

Continued over

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Company	Code	Price (current)	Price added to portfolio	Recommend- ation	Cap'n (\$M)	Date added	Portfolio Changes 20 July 2018
Clinuvel Pharmaceuticals	CUV	\$10.20	\$4.15	Spec Hold A	\$488	December 2014	IN:
Bionomics	BNO	\$0.480	\$0.295	Spec Buy A	\$232	March 2016	No changes
Volpara Health Technologies	VHT	\$0.765	\$0.375	Spec Buy A	\$176	June 2017	
Somnomed	SOM	\$2.060	\$0.94	Buy	\$128	January 2011	OUT:
Opthea	OPT	\$0.550	\$0.160	Spec Buy A	\$111	November 2014	No changes
Pharmaxis	PXS	\$0.310	\$0.260	Spec Buy A	\$99	December 2016	ito enanges
Osprey Medical	OSP	\$0.185	\$0.695	Spec Hold B	\$63	September 2015	
Visioneering Technologies	VTI	\$0.275	\$0.435	Spec Buy A	\$54	March 2017	
Micro-X	MX1	\$0.320	\$0.38	Spec Buy A	\$46	May 2017	
Factor Therapeutics	FTT	\$0.054	\$0.041	Spec Buy B	\$45	March 2018	
Adalta	1AD	\$0.295	\$0.23	Spec Buy A	\$30	July 2017	
Acrux	ACR	\$0.155	\$0.31	Spec Buy A	\$26	July 2017	
AirXpanders	AXP	\$0.085	\$0.745	Spec Buy B	\$24	September 2015	
MediBio	MEB	\$0.205	\$0.395	Spec Buy A	\$24	September 2017	
Rhinomed	RNO	\$0.160	\$0.320	Spec Buy B	\$19	December 2015	
Adherium	ADR	\$0.100	\$0.495	Spec Buy A	\$17	May 2016	
Dorsavi	DVL	\$0.100	\$0.480	Spec Buy B	\$17	December 2016	

What attracted Metters to Pharmaxis?

Over the last year Metters has been interacting with the research team at Pharmaxis. "They have a very deep understanding of what makes a good molecule. That's just years of experience. I've been impressed by the way that Pharmaxis has built outstanding relationships with KOLs and outside experts."

"Science can drive projects in different directions to the ones you anticipated when you first started. Part of being successful is having the flexibility to change course when the science is telling you something new."

While Pharmaxis does this well, one aspect that Metters assists the research team at Pharmaxis with, is with developing a stronger focus on understanding the needs for decision making in early development. This includes ensuring the right biomarkers are prepared for clinical trials.

What Puts Pressure on Big Pharma to do Deals?

"What's forcing Pharma to do deals is the recognition that they need to access external opportunities to fill their pipeline. For the most part, they can not develop enough internal opportunities to compensate for the accepted attrition rate in discovery, research and early development."

"I think the approach to look outside and work with biotech and academic centres is really healthy," she said. At Merck, Metters was explicitly supportive of increasing the company's ability to find and bring in external innovation. "Every Pharma is looking to do this, in different ways." It is still tough for biotechs (to work with Pharma) because company processes can be very different with each pharmaceutical company.

Metters believes that people from small biotechs need to build very long-term relationships and they need to work their way through a Pharma to find appropriate champions for their program, despite such a process always being arduous.

Is Big Pharma outsourcing More?

There has been a massive increase in outsourcing by Big Pharma to biotech over the last 10-15 years, according to Metters, who believes this trend will continue. "That's because Pharma is trying to reduce the investment and increase the success rate. In terms of chemistry, Pharma was the leader but now small research organisations provide most of the building blocks needed for R&D."

Metters believes there has been a tremendous improvement in the quality of assets that are now coming out of biotech, which has in part been driven by the movement of pharma executives into biotech, as Big Pharma has re-structured.

Demand for Translational Models

One area that is not outsourced and for which there remains a large need is for translational models that will improve the probability of clinical success. "There is tremendous scope in this area to make a difference," she said. Biomarkers are not off-the-shelf, and this can make a big difference for small companies if they can bring these things into Pharma, said Metters.

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How Biosha	ares Rates Stocks	Group B			
two categories.	e of valuation, Bioshares divides biotech stocks into . The first group are stocks with existing positive cash	Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.			
stocks without early stages of	to producing positive cash flows. The second group are near term positive cash flows, history of losses, or at commercialisation. In this second group, which are	<i>Speculative Buy – Class A</i> These stocks will have more than one technology, product or investment in development, with perhaps those same technologies			
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		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.			
	that investors may re-weight their holding by selling 75% of a stock.	Speculative Buy – Class B			
Group A	7570 01 a Stock.	These stocks may have more than one product or opportunity, and			
flows.	ting positive cash flows or close to producing positive cash	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.			
Buy Accumulate	CMP is 20% < Fair Value CMP is 10% < Fair Value	Speculative Buy – Class C			
Hold	Value = CMP	These stocks generally have one product in development and lack many external validation features.			
Lighten Sell	CMP is 10% > Fair Value CMP is 20% > Fair Value	Speculative Hold – Class A or B or C			
	t Market Price)	Sell			
-		tions, Opthea, ResApp, Pharmaxis, Dimerix, Cyclopharm,			
Adalta, Medi	ibio, Pharmaust				
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