

Subscribe
to
Bioshares

\$470/
48 issues

More details can be found
on the back page

Companies covered: ACW, AXP, CGS, IDT,
PYC

	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 - May '16)	33.0%
Year 16 (May '16 - current)	19.1%
Cumulative Gain	778%
Av. Annual gain (14 yrs)	18.8%

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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@bioshares.com.au

David Blake - Analyst
Ph: (03) 9326 5382
Email: blake@bioshares.com.au

Mark Pachacz - Analyst
Ph: 0403 850 425
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
\$440 (Inc.GST)
Edition Number 694 (5 May 2017)

Copyright 2017 Blake Industry and Market Analysis Pty Ltd. ALL RIGHTS RESERVED.
Secondary electronic transmission, photocopying, reproduction or quotation is strictly prohibited without written consent of the publisher.

Bioshares

5 May 2017
Edition 694

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

Extract from *Bioshares* –

Phylogica Charges Ahead!

Phylogica (PYC: \$0.046) is one of a small number of peptide chemistry companies globally possessing a novel chemistry platform, which in the case of Phylogica encompasses libraries of billions of peptides that are also enriched by a number of assays and techniques necessary for finding and optimising pharmaceutically useful compounds from these libraries.

The compounds that Phylogica has a proprietary interest in are peptides sourced from ancient bacteria. These peptides are a source of vast chemical diversity presenting applications in the discovery of druggable targets, to providing a source of peptides that block interactions between proteins, and also serving as intra-cellular carriers of drug payloads.

The company identifies its cell penetrating peptides as Functional Penetrating Phylomers (FPP).

Phylogica's share price has appreciated by more than 200% since early December 2016, when the company announced that its collaborators had received a \$750,000 NHMRC grant to fund research into the development of drugs which target both the Myc protein (see discussion below) and the cancer cell survival proteins Bcl-2 and Mcl-1.

Since then the company has also completed a board renewal process. Jeremy Curnock Cook has left the board; Dr Robert Hayes (formerly with Amgen and Janssen) and Dr Rick Kendall, Vice President Research at Kite Pharma and also formerly with Amgen, have joined the board. Company founder Dr Paul Watt changed roles, moving from his CSO position, to becoming Chief Scientific Advisor and a non-executive director.

The growth in the company's share price can also be attributed to an evolution in the company's business plan, which has been broadened from the provision of target validation services to more actively participating in the discovery and development of novel therapeutic solutions i.e. a drug product focus.

The company's CEO role remains unfilled although the company is in the process of looking to fill this position.

Targets Inside the Cell – Transcription Factors

Many drugs act on targets that exist outside a cell, for example, receptors located on the cell surface. Receptor-targeted drugs are designed to influence a communication pathway that often involves components inside the cell, such as transcription factors, which themselves are often shared with, or are common to, multiple signalling pathways.

Transcription factors play a key role in intra-cellular communication. Their role is to control gene expression e.g. the initiation of the process that begins with the reading of

Cont'd over

– *Phylogica cont'd*

a gene and the converting of the code into a protein. Transcription factors either suppress (down regulate) or promote (up-regulate) the expression process.

Examples of transcription factors are the estrogen receptor transcription factor, the hypoxia inducible factor (HIF), the heat shock factor (HSF), and the Hox, STAT, FOX and Myc families.

The Myc transcription factor is of great interest as a therapeutic target because it is found in about half of human tumours and is prevalent in leukemias and lymphomas. It has been found that cancer cells depend on it to survive and proliferate. In other words they have a unique dependency on Myc.

In normal cells, levels of Myc are tightly controlled. However, in cancer cells, this tight control dissipates so that its levels rise and its functions, especially those favouring replication and division, are directed to benefiting cancer cell proliferation and growth.

Myc's value as a target has been validated through investigations with the protein scaffold OmoMyc, which is being developed by Peptomyc (Spain).

OmoMyc works as an 'opposite' of Myc, being able to prevent Myc from binding with its natural ligand Max, and by filling a space in what is called the E-box with inactive elements of OmoMyc. In short, OmoMyc is a competitive blocker of Myc transcriptional activation.

Normal Myc is only up-regulated in blood stem cells. This means that when the over-expression of MYC is targeted, the potential, likely side effect is a decrease in blood cells (red, white and platelets).

According to Whitfield *et al* (2017), in their review article '*Strategies to Inhibit Myc and their Clinical Applicability*', "Multiple studies in mouse models of cancer demonstrated OmoMyc's therapeutic impact in different types of cancer, independently of their driving mutation or tissue of origin, pointing to a key role of Myc in tumorigenesis downstream of the diverse oncogenic lesions." And "Importantly in each model OncoMyc showed only minimal side effects, suggesting its safety and potential applicability in patients."

Phylogica believes it has discovered peptides that have a binding affinity for Myc comparable to OmoMyc.

Trapped in the Endosome

One of the problems encountered with other compounds capable of penetrating cell walls, and entering the nucleus has been that they become trapped in the endosome. For some of these of cell penetrating compounds, very large amounts of the compound must be delivered into the cell in order to get a sufficient quantity that can escape the endosome, a cell compartment which specialises in the sorting and processing of cellular material, as well as the destruction (endocytosis) of cellular material. However, a drawback with having to start with such large amounts of active drug is the potential for much higher costs, amongst other negative factors.

Phylogica has developed an assay, the Split-GFP complementation assay, which shows that its FPPs are better at escaping from the endosome compared to conventional CPPs (such as Tat and R9).

Intracellular Oncology Pipeline

Phylogica has developed a plan which not only includes developing an FPP+cargo construct targeting Myc in the indications of lymphoma, AML and breast cancer, but also intends to develop FPP conjugates against the Stat 5 transcription factor for AML and breast cancer, and against the YB1 transcription factor for AML and breast cancer.

The company anticipates selecting candidates for pre-clinical development in late 2017 or early 2018.

This selection process will be preceded by work to improve the potency of the compounds (which in some instances has been shown to be capable of reaching nanomolar levels) and the application of PASylation technology (as developed by XL-protein. Freising, Germany) to extend the half-life of the constructs. In the case of blood cancers such as AML, half-life extensions of up to 90 minutes may be all that is required. Initial studies performed to date have shown an increase of about 300% in the plasma elimination half-life of a PAS-conjugate.

Recent Developments

Phylogica's strategy is to validate the intracellular delivery of biologics (protein molecules) through a number of internal programs and partnering to the extent that they trigger transformational transactions.

Phylogica has developed its FPPs to be potent and potentially effective cell penetrating peptides and payload carriers. Continued validation of its FPP-myc and other FPP-payloads conjugates against other intracellular targets is likely to favour upward movements in its Phylogica's share price in the next 12 months, as confirmation of advances made to improve the potency, half-life and other pharmaceutical properties of its peptide-cargo constructs emerges.

Phylogica is capitalised at \$92 million and retained cash of \$7 million at March 31, 2017.

Bioshares recommendation: **Speculative Hold Class B**

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

Corporate Subscribers: Cogstate, Bionomics, Impedimed, Viralytics, Opthea, Reproductive Health Science, Innate Immunotherapeutics, Anantara Life Sciences, ResApp, Pharmaxis, Starpharma, Antisense Therapeutics, Dimerix, Cyclopharm, Adalta, Immuron, Medibio, Phylogica

Disclaimer:

Information contained in this newsletter is not a complete analysis of every material fact respecting any company, industry or security. The opinions and estimates herein expressed represent the current judgement of the publisher and are subject to change. Blake Industry and Market Analysis Pty Ltd (BIMA) and any of their associates, officers or staff may have interests in securities referred to herein (Corporations Law s.849). Details contained herein have been prepared for general circulation and do not have regard to any person's or company's investment objectives, financial situation and particular needs. Accordingly, no recipients should rely on any recommendation (whether express or implied) contained in this document without consulting their investment adviser (Corporations Law s.851). The persons involved in or responsible for the preparation and publication of this report believe the information herein is accurate but no warranty of accuracy is given and persons seeking to rely on information provided herein should make their own independent enquiries. Details contained herein have been issued on the basis they are only for the particular person or company to whom they have been provided by Blake Industry and Market Analysis Pty Ltd. The Directors and/or associates declare interests in the following ASX Healthcare and Biotechnology sector securities: Analyst DB: ACR,CGS,COH,CSL, CYC,FTT,IPD,PNV,NAN,OSP,SOM,UCM,VTI; Analyst MP: ADR, CGS,CIR,CUV,FTT,IDT,IIL,IPD,PXS,RNO,SOM,SPL,VLA.. These interests can change at any time and are not additional recommendations. Holdings in stocks valued at less than \$100 are not disclosed.

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **\$470**

For multiple email distributions within \$750 2-3 email addresses
 the same business cost centre, our \$1010 4-5 email addresses
 pricing structure is as follows: \$1280 6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for \$ _____ made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card \$ _____ MasterCard Visa

Card Number

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph () _____

Emails _____
