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From the Analysts

There are a number of milestones approaching for several local biotechs in the run up towards the end of this year. In this edition we look at some of these forthcoming value drivers.

Starpharma has hit one of those major milestones early, gaining European approval for Vivagel BV. The product is expected to be on pharmacy shelves within six months.

And Pharmaxis has provided more information around its Boehringer Ingelheim deal and the approaches it is taking to developing drugs to treat the emerging silent epidemic, NASH (fatty liver disease).

Companies covered: ACG, AXP, IIL, OSP, PXS, SPL

	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 14 (May '15 - current)	6.8%
Cumulative Gain	**492%**
Av. Annual gain (14 yrs)	**17.0%**

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Extract from Bioshares –

Pharmaxis Explains Different Approaches To NASH, Adds More Detail To BI Deal

This week Pharmaxis (PXS: $0.21) provided an update on its clinical R&D pipeline, discussed different approaches to treating NASH, and explained why NASH is a major health problem and drug development opportunity.

Two Approaches to Treating NASH

Pharmaxis has two approaches to treating NASH. The first is through inhibiting inflammation in the liver by blocking the semicarbazide-sensitive amine oxidase (SSAO) enzyme. This will likely be a treatment for NASH at an early stage of disease progression.

The second approach is to prevent scarring in the liver once inflammation has already occurred. The LOXL2 enzyme is essential in the body for cross linking collagen to form scar tissue. Pharmaxis is at the lead optimisation stage for a LOXL2 inhibitor for the treatment of NASH. This potential therapy will likely be used as a more advanced treatment than an SSAO inhibitor that Boehringer is commercializing.

Pharmaxis has also partnered its LOXL2 program with Synairgen for a different indication, in the treatment of idiopathic pulmonary fibrosis.

Boehringer Ingelheim Deal – A Recap

In May this year Pharmaxis signed what could be described as a company saving deal with Boehringer Ingelheim which saw Pharmaxis receive a cash injection of $41 million in upfront payments with a potential deal value of more than $750 million. Boehringer acquired the compound PXS4728A which will be developed firstly for the treatment of NASH (non-alcoholic steatohepatitis).

The view of Pharmaxis post the Boehringer deal is slowly changing, with US investment fund BVF continuing to increase its stake in the company.

Pharmaxis' Head of Drug Discovery, Wolfgang Jarolimek, described the company's approach to drug discovery and development, as well as providing more information of what made the compound developed by Pharmaxis so appealing to Boehringer.

The compound sold to Boehringer, PXS4728A, inhibits the SSAO enzyme. (PXS4728A is based on a template for drugs developed to inhibit monamine oxidases. Pharmaxis' 2008 patent for its SSAO/VAP-1 inhibitor refers to monamine oxidase inhibitors being used to treat Parkinson's disease, e.g selegiline and other CNS conditions.)

Pharmaxis' approach has been to work on validated targets, using small molecules, in diseases where plasma biomarkers can be easily measured, and secures early proof-of-

Cont'd over

concept work by conducting initial trials in Australia where the process can expedited.

Pharmaxis was able to move from the end of preclinical testing to start Phase I clinical studies within three months.

Features of PXS4728A

There were a number of features of PXS4728A that made it a compelling compound for Boehringer to acquire. The compound has very good bioavailability, with absorption into the blood stream very quick and peak concentrations being reached within one hour.

The half-life of the compound in the body is short, at less than two hours, but with inhibition of the target enzyme lasting for more than a day from a single 10mg dose. This means the compound can be delivered, absorbed, generate a lasting effect and leave the body, without the complications of co-administration with food.

Phase I trials have shown a clear dose dependent response, with increasing doses showing an increased lowering of the SSAO enzyme in the blood. At 24 hours, just one dose of the lowest concentration of 3mg of drug achieved a 70% reduction in SSAO levels. The next highest dose of 10mg achieved an 80% reduction at 24 hours which was the target level.

Results of Phase I Study

This week the company announced the final results from its Phase I study. It showed that when dosed over 14 days, once a day, that long lasting inhibition of the target enzyme SSAO was achieved and that the treatment was found to be safe and well tolerated by the volunteers in the study.

Jarolimek said that as a general rule-of-thumb, a dose below 10mg is generally a safe dose. That the drug has high bioavailability means there are less challenges for drug development.

Potential Payments

Pharmaxis stands to receive a further $80 million from Boehringer when the drug moves into Phase II and Phase III trials for the treatment of NASH. Phase II studies are expected to start in late 2016 or early 2017, at which point we estimate Pharmaxis will receive around one third of the $80 million in milestone payments.

Pharmaxis stands to receive over $750 million in total if the drug is approved or two indications and if certain sales milestones are achieved.

In addition, Pharmaxis is entitled to a earn-out royalty from sales, which starts at single digits and increases to double digits based on sales levels. The first indication is for NASH. The second indication may be for COPD.

Pharmaxis is continuing in-house drug development in a number of areas, including an SSAO/MAOB inhibitor for the treatment of neuro-inflammatory conditions including Alzheimer's disease and MS.

NASH – A Clinically Silent Disease

Professor Jacob George is a leading liver specialist at the University of Sydney. Professor George spoke at a briefing organised by Pharmaxis. He said that NASH is a rapidly building, silent, health epidemic for which there remains no effective treatment. The reason for the rise in this disease is due to the alarming levels of obesity in the western world. Just 25 years ago, the proportion of the population in the US defined as obese (a BMI greater than 30) was between 10%-15% in most states. But just five years ago, over 40 states had populations with more than 20% of people defined as obese.

The situation is not much better in Australia where one third of the population is affected by steatosis (fatty liver). When a fatty liver is combined with inflammation, it leads to NASH, which affects between 3%-5% of the population in Australia. From NASH, the liver disease can progress to cirrhosis. People with NASH and cirrhosis have a 20% probability of death within seven years according to Professor Jacob.

Professor Jacob said that NASH will be a major disease in the next two decades because of lifestyle and obesity. Awareness among general practitioners of NASH remains low because it is a clinically silent disease. New technology developed from the French cheese industry, called Fibroscan, is now being used to non-invasively measure scarring in the liver.

Around 90% of diabetics have NASH. Professor Jacob said that in general, a 10% drop in weight can resolve 90% of NASH cases. However, targeting fat to prevent liver disease has not worked. The next step is to target inflammation.

At the briefing, CEO Gary Phillips said the company is still a supplier of the respiratory drug Bronchitol, but that this drug had been partnered in most major regions.

Phillips said the Boehringer deal has been recognised as a big deal globally, with the company building quality programs with Phase I/II ready compounds that big pharma can invest in.

Pharmaxis is capitalised at $67 million. The company had $54 million in cash at the end of June.

Bioshares recommendation: **Speculative Buy Class B**

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 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, LBT Innovations, Tissue Therapies, Viralytics, Phylogica, pSivida, Benitec BioPharma, Invion, Imugene, Analytica, Circadian Technologies, Reproductive Health Science, Regeneus, Innate Immunotherapeutics, Anatara Life Sciences, ResApp, Pharmaxis, Starpharma