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Bioshares

19 September 2022
Edition 925

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

Companies covered: **CGS, IMU, MX1, PXS, RAP**

	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 - Current)	-1.1%
Cumulative Gain	1598%
Av. Annual gain (21 yrs)	19.0%

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Extract from Bioshares –

Pharmaxis: Can PXS-6302 'Un-scar the Scar'?

Pharmaxis (PXS: $0.084) is using its lysyl oxidase platform to develop a topical application for the removal of scars. Results are due around year's end and may be a driver for this stock over coming months.

Pharmaxis CEO Gary Phillips said that the company has the first-in-class and best-in-class compounds in this field. According to Phillips at an R&D day earlier this year, the reason why Pharmaxis has extended its R&D programs into scarring is because it's where the science has led the company to.

Phillips said that whilst there is a lot of investment being made into the development of wound healing products, there is very little that addresses scarring in development. He believes there is a strong demand for a pharmacological approach to treating scars with around 100 million people a year undergoing operations that result in scarring, together with the abundance of existing scars.

Dr Mark Fear, who works at the Burn Injury Research Unit at the University of Western Australia, explained that scar tissue occurs because of the build up of fibroblasts in the dermis (the layer below the epidermal surface layer of skin) which generates densely packed collagen. Even when the skin has remodelled after 18 months, the collagen turnover in the dermis continues for life.

The final step of collagen cross linking in the skin is catalysed by lysyl oxidase, which is the target that Pharmaxis is seeking to inhibit. This makes the skin (scar) very stable, largely insoluble, and very hard to remove according to Dr Fear. It is expected that PXS-6302 will initiate degradation of the collagen back to a soluble form, which Dr Fear believes should shift the balance back to normal skin.

Preclinical Data

In laboratory studies, PXS-6302 has shown to reduce the level of collagen as well as the level of collagen cross-linking. Dr Fear's group also assessed the penetration of PXS-6302 across a skin membrane in the laboratory and found the PXS-6302 cream was able to effectively penetrate the human skin sample, readily crossing the skin barrier. This is very important as delivery has been a major issue in developing an effecting treatment for scars.

Dr Fear's group has conducted testing with PXS-6302 in three preclinical models. The first was in a full-thickness wound that was generated and then treated with PXS-6302 for 28 days. The cross-linking in the collagen was significantly diminished in a dose dependent manner.

Continued over

The second study was in a porcine model using an excision injury (10cm^2 full thickness). The pigs were treated daily for 10 weeks. The improvement in the scars was dose dependent with independent, blinded review by a plastic surgeon.

The third study used a burn model. Treatment with PXS-6302 achieved an improved appearance, as well as slightly better pliability (softer skin) and similar tissue strength. Dr Fear said that the appearance and the pliability are the key properties of scars that matter to patients.

Dr Fear believes that due to the shift in collagen production, PXS-6302 has the potential to not just treat current wounds, but also existing scars because collagen is produced for a lifetime and PXS-6302 appears to reduce collagen production and collagen crosslinking in the dermis.

Professor Fiona Wood, also from the Burns Injury Research Unit at the University of Western Australia, said that scarring is a persistent mechanism. Dr Wood posed the question of "How can we un-scar the scar?" Dr Wood said with cell-based therapies, 80% of scolding scars can be returned to normal looking skin, however this does not deliver a truly regenerative process. Professor Wood said that the scar repair process used maintains a significant influence for life.

The body initiates an inflammatory response to heal but the extreme inflammatory response drives the poor scar outcome explained Professor Wood. The inflammation is worse the longer it takes for the wound to close, so reducing the time to healing will reduce the scar said Professor Wood. If the wound is healed within 10 days then scarring occurs in a very small percentage of cases. But if it takes 21 days to heal then 74% of people will have a scar for life from the wound.

Existing Treatments

Silicon sheeting is currently used to reduce scarring and works on some people some of the time. In around 8% of people it causes an adverse reaction. Laser therapy is also used to treat scars although is a coarse approach that needs to be finessed according to Professor Wood. Pressure garments can be effective for the short-term but the effectiveness is inconsistent. With injected steroid treatment, 50% of scars will return within the year. The above approaches make up the standard practices to reduce or treat scars.

Professor Wood said the Holy Grail is to "un-scar the scar". There needs to be an understanding of how the extracellular matrix (in the dermis) can be controlled to drive a regenerative process in the surface of the skin, not just in the short term.

Solaria 2 Trial - Part 1

In the Pharmaxis study which Professor Wood is coordinating, the first eight patients with scars were treated with PXS-6302 (2%) to a 10cm^2 area of an established scar (more than one year old). These patients were treated daily for 90 days, with a small skin biopsy at Days 1, 7, 28 and 90.

At the date of the R&D day, the first patients had reached the 60 day treatment point from Cohort 1. The next cohort of 42 patients are being randomised to receive either PXS-6302 or placebo.

Solaria 2 Trial - Part 2

The second trial will be investigating whether PXS-6302 can prevent scarring. Adults with non-burn wounds will be recruited at two to three weeks after injury (once the wound has initially closed) and treated daily with PXS-6302 for three months.

This will be a randomised control study. Professor Wood said that after six weeks it is clear which scars will cause issues, and as such, a three-month treatment period should be effective in assessing the potential benefit of PXS-6302. One of the secondary assessments will be how many patients will need to proceed to laser and steroid therapy.

Q&A

One of the questions Professor Wood and her team is seeking to answer is which type of scar is most receptive to treatment with PXS-6302. It is known that collagen turnover is more rapid in younger people so will the therapy be more beneficial for younger people? In these trials keloid scars are not being investigated (initially) because they are so difficult to treat. Dr Fear said there is definitely potential for PXS-6302 to be used to treat keloid scars but that would be done in a separate study.

Other information that will be obtained from the current study is mapping the collagen turnover in patients, how that changes with treatment with PXS-6302 and how that reflects treatment outcomes.

Professor Wood said that: **"Already in some quite complex scars there is an indication of improvement. You could feel and see a difference. My observation is that we will have an impact on scarring (in this study). At this point, our indication is that they (the scars) are responsive (in around half of the patients)."** What will need to be established is how long the treatment will be required, which in some scars may be three months rather than two months for instance, according to Professor Wood.

It is encouraging at this point, but the impact of the carrier cream may need to be considered, which will be determined in the randomised part of the study where all patients receive the carrier cream.

What would a good result look like in this study? Professor Wood said that if the patients want to continue with treatment and trial PXS-6302 in other areas then that is a successful result. Many of these patients have much larger scars with only a 10cm^2 area being treated. Given the scars are static, the impact of the treatment within the context of the larger scar will be visible (if any) for many of the patients according to Dr Fear.

From an objective measure, 3D scanning will be used to assess changes in the randomised study. In the first eight patients, effective inhibition of the target (lysyl oxidase) is being measured and found to be achieved said Dr Fear.

Inhibition of the lysyl oxidase lasts for a lengthy period because the enzyme is not synthesized very quickly according to Dr Fear.

Continued over

It will take weeks for full restoration of the enzyme following cessation of treatment.

Earlier this month Pharmaxis stated that recruitment into the 42-patient randomised study is now 60% complete. Results are due by year's end but may take slightly longer with recruitment yet to be completed and treatment lasting for 90 days.

Pharmaxis is capitalised at $46 million with a proforma cash balance at June 30 of $21 million.

Bioshares recommendation: **Speculative Buy Class A**

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 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, ResApp Health, Pharmaxis, Dimerix, Adalta, Patrys, Antisense Therapeutics, Imugene, Chimeric Therapeutics, Neuren Pharmaceuticals, Neurotech International, Aroa Biosurgery, Radiopharm Theranostics, Imricor Medical Systems, Anteris Technologies