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Pharmaxis (PXS)

Exploring efficacy in cancer and fibrosis

30 November 2021

Speculative Investment

Outperform

Our View

Pharmaxis has two FDA-approved respiratory drugs and a pipeline of drugs developed in house that are targeting fibrosis and inflammation. Two of its anti-fibrosis drugs, PXS-5505 and PXS-6302, are expected to read out initial efficacy data in H2 CY22 in the fibrotic bone marrow cancer myelofibrosis (MF), and in wound scars, respectively. It recently announced plans to expand clinical development of PXS-5505 into a second indication in liver cancer. At the completion of its current capital raise, PXS will have pro forma cash of ~$25m to support its clinical development program. Its two FDA approved respiratory products, Bronchitol for cystic fibrosis (CF) and the Aridol asthma diagnostic, are expected to be profitable on an ongoing basis and to contribute ~$10m of EBITDA by FY26. PXS's market cap of $55m is very modest for a company with a portfolio of revenue generating drugs and with clinical efficacy readouts in two indications expected next year. We see the potential for a significant rerate as PXS approaches the readout of initial clinical data for the MF and wound scar trials in H2 CY22. We initiate coverage with an Outperform recommendation and valuation of $174m or $0.31/sh fully diluted.

Key Points

PXS-5505 oral pan-LOX inhibitor - inhibits all of the lysyl oxidase (LOX) family of enzymes. PXS successfully completed a Phase 1c trial which tested 3 doses of PXS-5505 in MF patients. The drug was well tolerated, so treatment has commenced in a Phase IIa expansion cohort which will treat 24 patients for 6 months at the highest dose tested in the Phase Ic trial. While the primary endpoint is safety, the main efficacy endpoint, a reduction in fibrosis assessed by bone marrow biopsy, is expected to report in H2 CY22. In preclinical models, PXS-5505 showed potential to be an effective treatment for MF, stopping the progress of fibrosis which crowds out red blood cell production in the bone marrow. An initial clinical trial of PXS-5505 in a second indication, liver cancer, is in the final stages of preparation, after promising preclinical results.

PXS 6302, a topical pan-LOX inhibitor, is being trialled as a treatment for scar tissue, including burn scars, at the Fiona Stanley Hospital in Perth. In preclinical studies PXS-6302 treatment resulted in cosmetic and functional improvement to scarring. PXS-6302 has the potential to reduce the excessive scar formation that causes contraction of burn scars, to reduce the formation of keloid scars following surgery, and to help resolve existing scars.

Productive drug development pipeline.
PXS has developed a number of drug candidates based on its expertise in the chemistry of amine oxidase inhibitors. In addition to its pan LOX inhibitors, its pipeline includes selective Lysyl Oxidase Like inhibitors (LOXL2) targeting chronic fibrotic diseases, and a semicarbazide-sensitive amine oxidase (SSAO) inhibitor PXS-4728. PXS outlicenced PXS-4728 to Boehringer Ingelheim (BI), receiving payments of A$83m. BI abandoned development of PXS-4728 due to dose dependent drug interactions, and returned the rights to PXS in 2020.

Bronchitol and Aridol. After a long delay, PXS's Bronchitol CF treatment gained FDA approval in October 2020, adding to approvals in Australia, Europe and Russia. PXS manufactures Bronchitol and related product Aridol at its facility in Sydney. The mannitol respiratory business lost ~$4m in FY20, but is expected to be cash flow positive going forward. PXS is streamlining the mannitol business and sold distribution rights for Bronchitol in Russia and Bronchitol and Aridol in Australia for $4M in 2021. Its US partner Chiesi anticipates peak sales of Bronchitol in the US to be ~US$50m/yr; ~20% of this amount would flow through to PXS's pre-tax earnings. Management estimates that the mannitol business could generate ~$10m of EBITDA by FY26.

Summary (AUD)

Market Capitalisation	**$55M**
Share price	**$0.105**
52 week low	$0.071
52 week high	$0.16
Cash as at 30 September 2021	$16.1m

Share price graph (AUD)

Historical Financials (AUDm)

	FY21A	FY22E	FY23E
Revenue ($m)	23.7	14.6	14.0
R&D ($m)	(8.4)	(10.7)	(9.1)
SG&A ($m)	(4.2)	(4.2)	(4.3)
EBITDA ($m)	(0.2)	(11.0)	(10.8)
Reported NPAT ($m)	(3.0)	(13.0)	(12.7)
NPAT Adj. ($m)	(3.0)	(13.0)	(12.7)
EPS Adj. (c)	(0.7)	(2.9)	(2.8)
PE ratio (x)	n/a	n/a	n/a
DPS (c)	0.0	0.0	0.0
EV/Sales	2.1	3.5	3.6
EV/EBITDA (x)	n/a	n/a	n/a
ROE	n/a	n/a	n/a

Pharmaxis - Summary of Forecasts — PXS $ 0.105

PROFIT & LOSS SUMMARY (A$m)

Year end June	FY21A	FY22E	FY23E	FY24E
Mannitol segment revenue	22.7	10.4	10.4	14.7
Other royalties, milestones	0.4	0.0	0.0	0.0
Other (incl. R&D tax incentive)	0.6	4.3	3.6	3.4
Total Revenue	**23.7**	**14.6**	**14.0**	**18.1**
Growth (pcp)	817%	-38%	-4.2%	29.0%
Mannitol segment expenses	(11.2)	(10.8)	(11.4)	(12.1)
R&D Expenses	(8.4)	(10.7)	(9.1)	(8.5)
Corporate & other expenses	(4.2)	(4.2)	(4.3)	(4.5)
EBITDA	**(0.2)**	**(11.0)**	**(10.8)**	**(7.0)**
Dep'n/Amort'n	(3.2)	(1.9)	(1.3)	(0.9)
EBIT	(3.3)	(12.9)	(12.1)	(7.9)
Net Interest	(0.4)	0.2	0.1	0.0
NovaQuest Payments	0.0	(0.4)	(0.7)	(1.4)
Pre-Tax Profit	(3.0)	(13.0)	(12.7)	(9.3)
Tax Expense	0.0	0.0	0.0	0.0
NPAT Adj.	**(3.0)**	**(13.0)**	**(12.7)**	**(9.3)**
Growth (pcp)	n/a	n/a	n/a	n/a
Adjustments	0.0	0.0	0.0	0.0
NPAT Reported	(3.0)	(13.0)	(12.7)	(9.3)

PER SHARE DATA

Year end June	FY21A	FY22E	FY23E	FY24E
EPS (c) - Reported	**(0.7)**	**(2.9)**	**(2.8)**	**(2.0)**
Growth (pcp)	n/a	n/a	n/a	n/a
EPS (c) - Adjusted	(0.7)	(2.9)	(2.8)	(2.0)
Growth (pcp)	n/a	n/a	n/a	n/a
Dividend (c)	0.0	0.0	0.0	0.0
Franking	0.0	0.0	0.0	0.0
Gross CF per share (c)	0.8	(2.9)	(2.1)	(1.4)
NTA per share (c)	0.4	(0.5)	(3.2)	(3.0)

KEY RATIOS

Year end June	FY21A	FY22E	FY23E	FY24E
Net Debt : Equity (%)	-400%	642%	-23%	1%
Net Debt: EBITDA (x)	65.0	0.6	(0.3)	0.0
Current ratio (x)	3.2	4.8	2.4	3.1
ROE (%)	-139%	-1433%	179%	72%
ROIC (%)	36%	116%	99%	50%
Dividend Payout Ratio (%)	n/a	n/a	n/a	n/a

VALUATION MULTIPLES

Year end June	FY21A	FY22E	FY23E	FY24E
PE Ratio (x)	**n/a**	**n/a**	**n/a**	**n/a**
Dividend Yield (%)	**0.0%**	**0.0%**	**0.0%**	**0.0%**
EV/Sales (x)	2.1	3.4	3.6	2.8
EV/EBITDA (x)	n/a	n/a	n/a	n/a
EV/EBIT (x)	n/a	n/a	n/a	n/a

CAPITAL RAISING ASSUMPTIONS

Year end June	FY21A	FY22E	FY23E	FY24E
Shares Issued (m)	57.6	87.6	0.0	50.0
Issue Price (A$)	0.07	0.11	0.00	0.20
Gross Cash Raised (A$m)	4.3	9.2	0.0	10.0

BALANCE SHEET SUMMARY

Year end June	FY21A	FY22E	FY23E	FY24E
Cash	18.7	13.9	4.3	7.5
Receivables	3.0	4.3	3.6	3.4
Inventories	3.6	1.6	1.7	1.8
Other	0.0	0.0	0.0	0.0
Total Current Assets	25.3	19.8	9.7	12.7
Inventories	0.0	0.0	0.0	0.0
Property Plant & Equip	6.2	4.5	3.1	2.2
Intangibles	1.1	1.1	1.1	1.1
Other	0.9	0.9	0.9	0.9
Total Current Assets	8.3	6.5	5.2	4.2
TOTAL ASSETS	**33.6**	**26.3**	**14.9**	**17.0**
Accounts Payable	3.8	0.0	0.0	0.0
Borrowings	3.1	3.1	3.1	3.1
Employee benefit obligations	1.1	1.1	1.1	1.1
Other	0.0	0.0	0.0	0.0
Total Current Liab	7.9	4.1	4.1	4.1
Borrowings	4.3	4.3	4.3	4.3
Provisions	0.1	0.1	0.1	0.1
Other	27.2	27.2	27.2	27.2
Total Non-Current Liab	22.9	22.9	22.9	22.9
TOTAL LIABILITIES	**30.7**	**27.0**	**27.0**	**27.0**
TOTAL EQUITY	**2.8**	**(0.7)**	**(12.1)**	**(10.0)**

CASH FLOW SUMMARY

Year end June	FY21A	FY22E	FY23E	FY24E
EBIT (excl Abs/Extr)	**(3.3)**	**(12.9)**	**(12.1)**	**(7.9)**
Add: Dep'n & Amort'n	3.2	1.9	1.3	0.9
Other non-cash items	(12.7)	(2.3)	(4.6)	(2.8)
Less: Tax paid	0.0	0.0	0.0	0.0
Net Interest	0.1	0.2	0.1	0.0
Change in Rec.	4.1	(1.3)	0.6	0.3
Change in Inv.	(1.0)	2.0	(0.1)	(0.1)
Gross Cashflows	3.1	(13.3)	(9.6)	(6.2)
Capex	(0.6)	(0.1)	0.0	0.0
Free Cashflows	2.7	(13.4)	(9.6)	(6.2)
Share Issue Proceeds	4.1	8.6	0.0	9.4
Other	(2.9)	0.0	0.0	0.0
Dividends Paid	0.0	0.0	0.0	0.0
Net Cashflows	**3.9**	**(4.8)**	**(9.6)**	**3.2**
FX Effect on Cash	0.0	0.0	0.0	0.0

PXS base case valuation summary

	Probability (%)	Valuation (A$m)	Valuation (A$/share)
PXS-5505 in myelofibrosis	15%	81.6	0.15
PXS-6302 in wound scarring	15%	50.0	0.09
Mannitol respiratory business	100%	45.0	0.08
SG&A	-	(16.8)	(0.03)
Portfolio total	-	159.9	0.30
Cash (end FY22e)	-	13.9	0.03
Total Valuation	-	173.8	0.32

Overview

Pharmaxis is an Australian drug development company focused on inflammation and fibrosis (including fibrotic cancers) with a portfolio of products at various stages of development, including approved, marketed products. Its manufacturing and research facilities are based in Sydney, Australia.

Its drug pipeline is based on its expertise in the chemistry of amine oxidase inhibitors and includes:

- PXS-5505 oral pan-Lysyl Oxidase (LOX) inhibitor targeting myelofibrosis and other fibrotic cancers, including liver cancer
- PXS-6302 topical pan-LOX inhibitor targeting scarring after accidents, surgery and burns
- PXS-5382 selective Lysyl Oxidase Like (LOXL2) inhibitor targeting chronic fibrotic diseases including kidney fibrosis, pulmonary fibrosis, liver fibrosis (NASH) and cardiac fibrosis
- PXS-4728 semicarbazide-sensitive amine oxidase (SSAO) inhibitor, repurposed for neuro inflammatory diseases (previously partnered with Boehringer Ingelheim for non-neurological inflammatory conditions such as NASH)
- PXS-4699 in preclinical development for Duchenne muscular dystrophy (DMD)

PXS also has two FDA-approved marketed drugs based on inhaled dry powder mannitol that are manufactured at is purpose-built facility in Sydney:

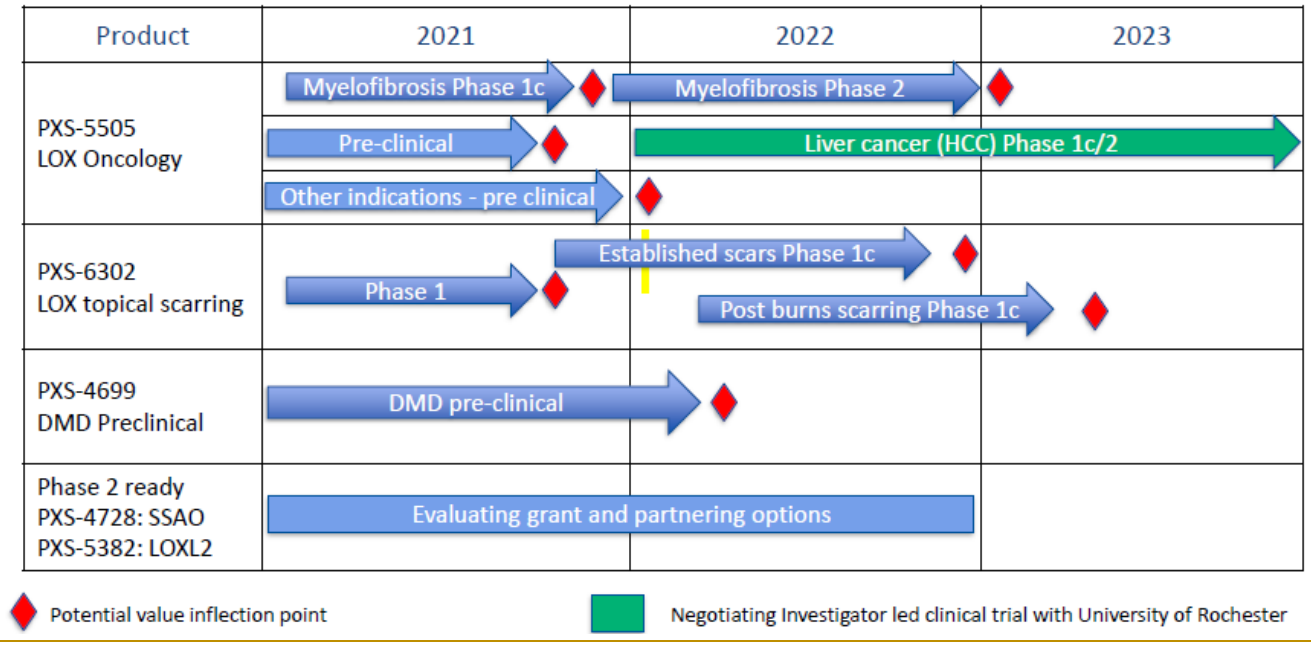
- Bronchitol for cystic fibrosis, which is approved and sold in the US, Europe, Russia and Australia.
- Aridol lung function test for asthma is approved and sold in the US, Europe, Australia and Asia.

Exhibit 1 highlights some of the potential valuation inflection points for the company over the next two years. We expect to see meaningful efficacy readouts from the two lead pan-LOX programs in H2 CY22.

While we do not discuss PXS-5382, PXS-4728, PXS-4699 or the amine oxidase inhibitor discovery program in detail in this report, they are important potential sources of future value creation for the company.

Pharmaxis's drug development pipeline is protected by a portfolio of patents, including composition of matter patents, with an average life of around 20 years, in all major territories. The key patent families, WO2020024017 covering PXS-5505 and WO202101201 covering PXS-6302, have earliest expiries of 2038 and 2039, respectively.

Exhibit 1: Pharmaxis' drug development pipeline



Source: Pharmaxis.

Financial Summary

PXS has a strong balance sheet to support development of its dug pipeline. It had $16.1m cash on 30 September and on 17 November it announced a $7.2m institutional placement and a share purchase plan to raise approx. $2m from eligible shareholders. If fully subscribed, the capital raise would increase pro forma cash to ~$25m. PXS also has a $19.9m liability under the NovaQuest financing agreement, but this facility is not repayable other than as a percentage (approx. 6-7%) of US Bronchitol revenue over a period of up to 7 years (expiring 31 March 2028).

PXS reported a loss of $3.0m in FY21 compared to a loss of $13.9m the previous year. The improvement was due $16m of revenue from Bronchitol milestone payments and the sale of Bronchitol distribution rights in Russia. Operating cash flow was positive $3.1m in FY21, compared to $13.2m cash outflow in FY20.

Operating expenses decreased slightly in FY21 to $23.8m vs 24.7m in FY20. Expenditure in FY21 comprised $11.2m in the mannitol business segment, $8.4m on new drug development and $4.2m in corporate overheads. With revenue of $6.7m from mannitol sales and $16.0m in milestone payments and distributor appointment fees, the operating result in mannitol segment improved to $11.5m in FY21 compared to a $4.0m EBITDA loss in the previous year. With expenditure expected to be reduced by ~$1m following the sale of Russian distribution rights in April and increased revenue from US Bronchitol sales, the Mannitol segment is expected to be profitable on an ongoing basis, and expected to generate EBITDA of ~$10m by FY26.

Initial target for PXS-5505 is the rare bone cancer myelofibrosis

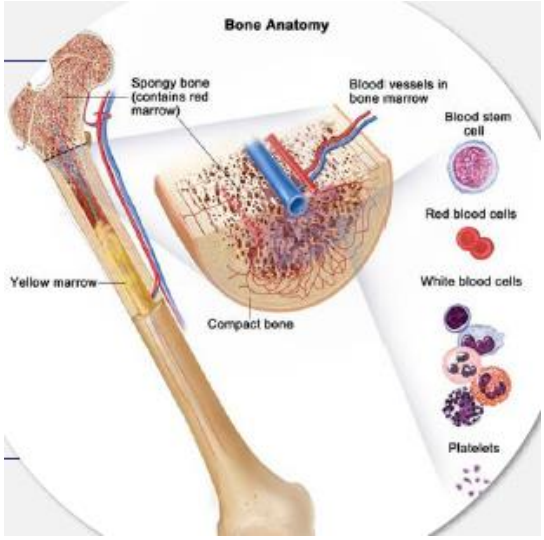
MF is a disorder in which normal bone marrow is gradually replaced by fibrous scar tissue, leading to progressive bone marrow failure over time. Exhibit 2 shows the normal anatomy of bone marrow, which produces red and white blood cells and platelets. In MF, high levels of growth factors overstimulate fibroblasts, resulting in overgrowth of thick fibres that gradually replace the normal bone marrow tissue. This prevents the production of adequate numbers of red cells, white cells and platelets, resulting in anaemia, low platelet counts, and production of blood cells in areas outside the bone marrow, such as the spleen and liver, which become enlarged as a result.

MF is usually diagnosed later in life, between ages of 60-70 years. While the cause of MF is largely unknown, it is driven by clonal mutations of hematopoietic stem cells, including mutations of the JAK, MPL and CALR genes. It can be classified as either JAK2 mutation positive or negative.

Myelofibrosis is an uncommon disease, with the annual incidence of primary MF estimated to be approximately 0.5-1.5 cases per 100,000 individuals in the US. Estimates of annual incidence in Europe range from 0.1 to 1.0 cases per 100,000 individuals per year. The total prevalence in the US is estimated to be between 16,000 and 18,500 patients.

PXS-5505 was granted Orphan Drug Designation for MF by the FDA in July 2020, in recognition of the unmet need in this condition. The designation brings seven years of market exclusivity in the US for use in these indications, a waiver of FDA fees, clinical trial protocol assistance and other incentives.

Exhibit 2: Normal bone marrow anatomy



Source: Pharmaxis.

PXS-5505 Phase IIa trial in MF underway

PXS has successfully completed a Phase Ic dose escalation study, in which 3-6 MF patients at each of 3 escalating dose levels were dosed with PXS-5505 for 28 days, with a starting dose level of 100 mg twice daily. PXS-5505 was well tolerated, with no safety signals identified. The highest dose inhibited the target LOX and LOXL2 enzymes by more than 90% over a 24-hour period at day 7 and day 28, as shown in Exhibit 4. Based on pre-clinical work the other LOX family enzymes (LOXL1, 3 and 4) are expected to be inhibited to a similar degree.

In October PXS announced that it had commenced dosing in the Phase IIa clinical trial of PXS-5505 in patients with MF (NCT04676529). The trial will treat 24 patients for 6 months at the highest dose tested in the Phase Ic trial. The first patients to enter the Phase II trial were subjects who participated in the in the Phase Ic dose escalation study. Recruitment of additional subjects is underway at trial sites in Australia and Korea, with additional sites to be progressively opened in other countries, including the US. The company expects to complete the study by the end of 2022.

The trial aims to demonstrate that PXS-5505 is safe and well tolerated in MF patients who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs. Secondary efficacy endpoints will explore the effect of PXS-5505 on important disease parameters including bone marrow fibrosis, cytopenia and spleen volume. The trial is being conducted under an IND that was cleared by the US FDA in August 2020.

Independent research has shown that several LOX family enzymes are upregulated in MF. Importantly, the degree of LOX inhibition in the Phase Ic study exceeds the levels that caused disease modifying effects in the company's studies in preclinical models of MF. These effects included improvements in blood cell count, diminished spleen size, and reduced bone marrow fibrosis. Exhibit 3 illustrates the reduction of bone marrow fibrosis following PXS-5505 treatment in a mouse model of MF.

Exhibit 3: PXS-5505 reduces reticulin fibrosis in primary myelofibrosis mouse model

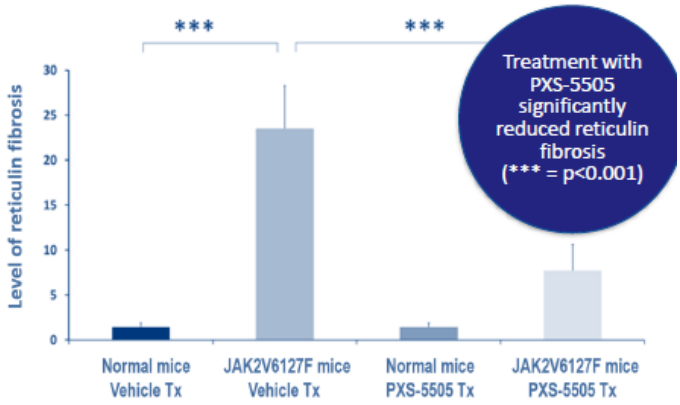
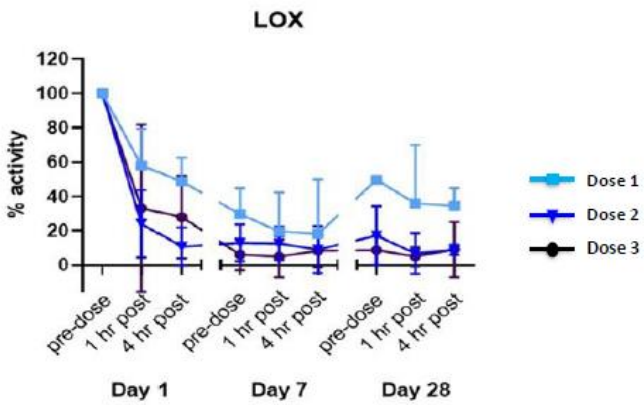


Exhibit 4: Phase Ic dose escalation in MF patients showing degree of LOX enzyme inhibition



Source: Pharmaxis.

PXS-5505 – liver cancer

While the company's primary focus for the development of PXS-5505 is in MF, the drug also has potential in other fibrotic cancers including myelodysplastic syndrome, liver and pancreatic cancers, melanoma and glioblastoma.

PXS recently announced that the FDA has cleared an Investigational New Drug (IND) application for a Phase II trial of PXS-5505 added to Standard of Care in hepatocellular carcinoma (HCC), although the timing of the trial is yet to be finalised. The IND was submitted by the University of Rochester, New York, which will lead the trial. The trial will treat patients who have newly diagnosed, unresectable HCC for 6 months with PXS-5505 added to a combination of a PD-L1 inhibitor and an anti-VEGF drug, eg Keytruda plus Avastin. The estimated cost of the investigator led trial is ~US$2.5m

HCC is the most common type of primary liver cancer, which is the 4th leading cause of cancer deaths worldwide, with a poor 5-year survival rate of 19.5%. HCC is characterised by the presence of highly fibrotic tissue that increases tumour stiffness and decreases the penetration of anti-cancer drugs.

The planned clinical trial in HCC patients is supported by the results of preclinical studies at the University of Rochester in cholangiocarcinoma (CCA), the second most common form of primary liver cancer. The studies showed that LOX enzymes are significantly elevated in CCA tumour tissue specimens and correlates with poor prognosis. Secondly, they showed in preclinical models that the combination of PXS-5505 and chemotherapy significantly improves survival, delays tumour growth and reduces intratumoural pressure.

The market for liver cancer drugs is estimated to be worth US$2bn and is projected to grow to US$7bn by 2027.

PXS-6302 – treating excessive wound scarring

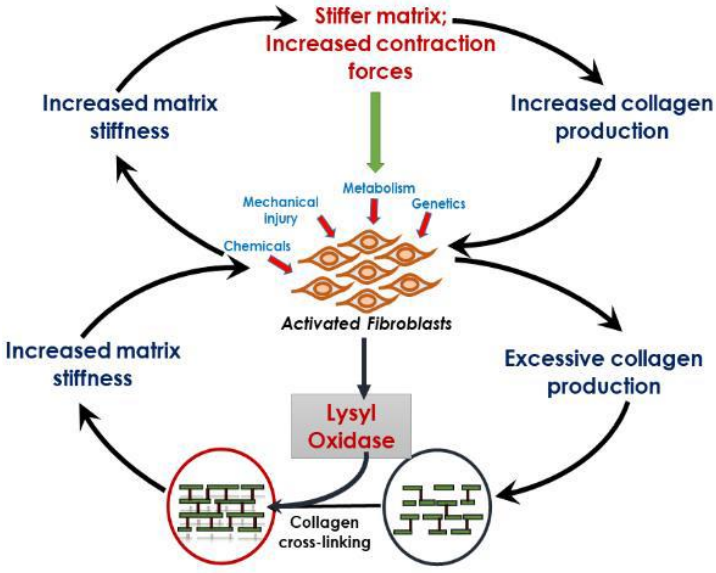
PXS has developed a pan-LOX inhibitor drug formulation for topical application with potential for use in scar revision, keloid scarring and scarring from burn wounds. The drug, PXS-6302, has shown promising preclinical results, inhibiting the enzymes that play a critical role in the development of scar tissue. Preclinical studies also showed that treatment with PXS-6302 monotherapy results in cosmetic and functional improvement to scarring. The role that lysyl oxidase (LOX) plays in keloid scar formation is illustrated in Exhibit 5.

A Phase Ia trial of PXS-6302 for one month in healthy volunteers showed good tolerability and full inhibition of LOX in the skin. A 3-months study of PXS-6302 vs placebo in patients with established scars is expected to commence in the current quarter. A study to investigate PXS-6302 in scarring subsequent to burn injuries is expected to follow in 2022. Each patient acts as their own control, with one part of the scar treated with PXS-6302 and another part treated with placebo. The trial is being conducted by a group of researchers from the University of Western Australia (UWA) led by Professor Fiona Wood AM, and the Fiona Stanley Hospital. PXS is contributing to the cost of the trial.

Hypertrophic and keloid scars significantly affect patients' quality of life. Based on preclinical studies, the company is hopeful that PXS-6302 will arrest the scarring process, allowing the ongoing remodelling process to effectively melt the scar away. There are no drug treatments for scars in regular use. Common treatment regimens include silicone sheets and pressure, laser therapy and corrective surgery.

If PXS-6302 shows evidence of efficacy in the Phase II trial, we would expect it to attract interest from companies that are active in the dermatology space such as Galderma and Leo Pharma, or the Botox company Allergan (owned by AbbVie). We estimate that there is a sizable addressable market for the treatment or prevention of excessive scarring. In the US there are 40,000 hospitalisations are related to burn injuries each year, while the estimated incidence of keloid scars of 0.1% would represent a further 330,000 potential patients.[1]

Exhibit 5: Schematic of collagen turnover in keloid scars



Source: Pharmaxis

Mannitol-based respiratory products

Pharmaxis has two approved and marketed products based on inhaled dry powder from of the sugar mannitol that it manufactures and exports from a manufacturing facility in Sydney, namely:

- Bronchitol, an inhaled dry powder treatment for cystic fibrosis, which is approved and sold in the US, Europe, Russia and Australia.
- Aridol lung function test for asthma and to test for hypersensitivity to Bronchitol is approved and sold in the US, Europe, Australia and Asia.

[1] L. Téot et al. (eds.), *Textbook on Scar Management*, https://doi.org/10.1007/978-3-030-44766-3_5

Bronchitol helps CF patients clear the thick sticky mucous that otherwise accumulates in the lungs and makes them susceptible to lung infections. The main competing products that aid mucous clearance are the inhaled enzyme drug Pulmozyme (dornase alfa) and inhaled hypertonic saline. Antibiotics are another important tool for reducing lung infections in CF patients.

In the past decade there have been a number of drugs approved that address the genetic mutations that are the underlying cause of CF, but each drug only addresses a limited subset of CF mutations. Examples of this class of drugs include Kalydeco (ivacaftor), Orkambi (lumacaftor and ivacaftor) and Trikafta (elexacaftor, ivacaftor and tezacaftor). While these drugs have substantially improved outcomes for many CF patients, they do not compete directly with Bronchitol.

Bronchitol gained regulatory approval in Australia in 2011 and in Europe in 2012. In 2013 the FDA rejected the marketing application for Bronchitol and asked PXS to conduct a third Phase III trial. PXS subsequently licensed the US marketing rights to Bronchitol to Chiesi, a global pharmaceutical company headquartered in Parma, Italy, which substantially funded the additional Phase III trial. Bronchitol gained FDA approval on 30 October 2020 and was launched in the US market in Q1 CY21. PXS received US$10m (A$13.8m) in milestone payments in FY21 for the FDA approval and shipment of launch stock. Three sales milestones totalling US$15m are payable on achieving annual sales thresholds.

PXS receives revenue from the US market equal to about **30%** of Chiesi net sales, comprising a revenue share (similar to a royalty) in the high teens and a cost plus price for Bronchitol, which is exclusively manufactured by PXS in Sydney. After deducting 2-3% for the variable cost of manufacture of additional units of Bronchitol and 6-7% of US Bronchitol sales payable to NovaQuest under its financing agreement, approximately 20% of US net sales will flow thought to the bottom line of the mannitol business segment, (23% at the EBITDA level, 20% at the pre-tax profit level). Chiesi anticipates peak sales of ~US$50m in the US market, based on penetration rates seen in other markets.

PXS has also appointed Chiesi as its exclusive distributor in the UK, Ireland, Italy, Germany, Norway, Sweden, Finland, Denmark, Cyprus, Greece and Spain. In April 2021 PXS sold the sold distribution rights for Bronchitol in Russia for $2m to Turkish pharma specialty company GEN İlaç ve Sağlık Ürünleri San. ve Tic. A.Ş. In July 2021 it sold the distribution rights for Bronchitol and Aridol in Australia, New Zealand, and several Asian territories to Bioimpact Pty Ltd, a subsidiary of BTC Health Ltd (BTC.ASX) for $2m.

The mannitol business segment reported positive EBITDA of $11.5m in FY21, thanks to $16m revenue from milestone payments and the sale of distribution rights. Putting this non-recurring revenue to one side, sales revenue of $6.7m ($5.2m for Bronchitol and $1.4m for Aridol) combined with expenses of $11.2m resulted in an underlying EBITDA loss of $4.5m. Guidance is that the sale of the Russian distribution rights will reduce expenses by ~$1m, giving a pro forma underlying EBITDA loss of $3.5m. If US Bronchitol sales reach US$50m by FY26, in line with Chiesi's expectations, contributing ~US$10m (~A$13.3m) of EBITDA, then the mannitol segment should return positive EBITDA of ~A$10m by that time.

Fibrosis drugs such as PXS-5382 are of great interest to potential partners

Over the past few years big pharma has been quite active in deals for early stage assets in the fibrosis space. This suggests that PXS may be able to look at potential licensing or co-development options for the clinical development of its drug candidate PXS-5382 for fibrotic disease indications, in a similar manner to its earlier licence deal with Boehringer Ingelheim for PXS-4728.

Exhibit 6: Deals for early stage fibrosis assets

Acquirer	Target company	Indication	Deal type	Date	Stage	Upfront (US$m)	Potential (US$m)
Abbvie	Morphic Therapeutics	IPF/ fibrotic disease	Option exercise	Aug-20	Preclinical	20	n/a
AstraZeneca	Redx	IPF/ fibrotic disease	Licence	Aug-20	Preclinical	17	380
Novartis	Pliant Therapeutics	liver- NASH	Licence	Oct-19	Phase I	80	n/a
Boehringer Ingelheim	Bridge Biotherapeutics	lung- IPF	Licence	Jul-19	Phase I	50	1,200
Boehringer Ingelheim	Yuhan Corp	liver- NASH	Licence	Jul-19	Preclinical	40	830
AbbVie	Morphic Therapeutic	Fibrosis indications	Option to licence	Oct-18	Preclinical	100	n/a
United Therapeutics	Samumed	lung- IPF	US licence	Sep-18	Phase I	10	340
AstraZeneca	Ionis Pharmaceuticals	liver- NASH	Licence	Apr-18	Preclinical	30	300
Undisclosed	Oraxion Therapeutics	kidney- FSGS	Option to licence	Feb-18	Preclinical	n/a	125
Novartis	Conatus	liver- NASH	Licence	Dec-16	Phase II	50	650
Roche	Adheron Therapeutics	lung- IPF	Acquisition	Sep-15	Phase I	105	475
Boehringer Ingelheim	Pharmaxis	liver- NASH, eye	Asset purchase	Mar-15	Phase I	A$40	A$750+

Source: Taylor Collison. Note: IPF= idiopathic pulmonary fibrosis; NASH= non-alcoholic steatohepatitis, FSGS= focal segmental glomerular sclerosis

Pharmaxis's market cap compares favourably to comparable ASX-listed companies

The table below compares the market cap of PXS to a number of other pre-clinical, Phase I or early Phase II companies listed on the ASX. The market cap of PXS is considerably lower than most of the other stocks that are at a similar state of development, despite the fact that it has two FDA approved drugs. We see the opportunity for a significant re-rating of the stock as PXS approaches the initial efficacy data readouts for the Phase II trials of PXS-5505 and PXS-6302 in H2 CY22.

Exhibit 7: Selected Preclinical, Phase I or early Phase II companies listed on the ASX

Company	Ticker	Cash (A$m)	Mcap (A$m)	Notes
Patrys	PAB	5.9	68.6	Plans Phase I trial for lead candidate PAT-DX1 in H2CY22. DNA damage repair in cancer
Adalta	1AD	6.8	20.1	Lead drug AD-214 targets fibrosis (CXCR4). Phase I trial completed in healthy volunteers. Preparing for Phase II trial of an inhaled version of AD-214 in idiopathic pulmonary fibrosis (IPF)
Vectus Biosystems	VBS	4.6	43.6	Phase I trial for VB0004 underway. Anti-hypertensive and anti-fibrotic
Recce Pharmaceuticals	RCE	18.6	143.4	Phase I trials of its novel antibiotic R327 underway. Initial targets sepsis and wound infections
Noxopharm	NOX	23.6	130.0	Phase I/II study of idronoxil plus ^{177}Lu- PSMA-617 in prostate cancer completed. Phase I/II trial of idronoxil plus external beam radiotherapy in preparation.
Chimeric Therapeutics	CHM	17.4	56.7	Phase I trial of CLTX Chlorotoxin CAR T cell therapy for glioblastoma underway.
Phylogica	PYC	45.6	429.4	Pre-clinical cell penetrating peptide technology. IND filing for lead product VP-001 in inherited retinal disease planned for mid-2022 (earlier stage of development than the companies above).
Amplia Therapeutics	ATX	3.2	27.9	Focal Adhesion Kinase (FAK) inhibitor. Preparing for Phase II study of AMP945
Invion	IVX	2.9	115.4	INV001 Photodynamic Therapy for treating skin cancers in proof of concept pre-clinical studies (earlier stage of development than the companies above).
Pharmaxis	PXS	16.1	54.9	While PXS has an out-licenced FDA-approved drug, Bronchitol, its pipeline is focused on early Phase II development of its anti-fibrosis drugs PXS-5505 in cancer and PXS-6302 in burn scars.

Source: Taylor Collison research.

Risks

Pharmaxis is subject to clinical trial, regulatory and commercialisation risks common to all biotech companies. The key sensitivity is clinical progress of PXS-5505 and PXS-6302, and the safety and efficacy of the drugs. Off-target effects can result in severe adverse events that can stop drug development. Inadequate safety or efficacy can result in failure to recruit patients into studies, failure to partner and fund the program, failure to gain regulatory approval, or failure to be adopted for use by prescribing doctors once approved.

PXS had $16.1m cash at 30 September and raised $7.2m (before costs) in a placement in November. An ongoing share purchase plan aims to raise a further $2m. This ensures that PXS will be fully funded until after it reports initial efficacy data for PXS-5505 and PXS-6302 in H2 CY22. However, it would require a partnership or alternative forms of funding to advance these drugs into pivotal studies. There is no guarantee that the funding will be available on acceptable terms.

PXS is reliant on its marketing partners for the successful commercialisation of Bronchitol and Aridol. If these partnerships do not generate the expected revenues, then that would increase the company's reliance on external sources of funding to support development of its product pipeline.

Valuation

We initiate coverage of PXS with a valuation of $174m or 32c per share (undiluted), based on a risk-adjusted discounted cash flow model, which includes our estimates of the future milestone payments and royalty streams for PXS-5505 and PXS-6302 and revenue streams from the mannitol business segment, as listed in Exhibit 8. On a fully diluted basis, our valuation is 31c per share, after taking into account the options and performance rights on issue.

We have extended our cash flow forecasts out to 2040, in line with its existing patent portfolio, but assume that sales will decline by 10% per year from 2036 onwards. The Orphan Drug designation by the FDA brings seven years of market exclusivity for PXS-5505 for the MF indication in the US; if it gains ODD in the EU then it would gain ten years of market exclusivity in Europe. We assume a long-term exchange rate of US$0.75/A$ and apply a 12.5% discount rate for the pipeline drugs and 10% for the marketed drugs in the mannitol business segment.

We model PXS out-licensing global rights to PXS-5505 and PXS-6302 in separate transactions in FY24, although we note that under an alternative strategy PXS may choose to raise additional funds to progress the drugs into late stage clinical development itself.

We assume that the PXS-5505 licence deal includes an upfront payment of US$85m and US$540m of milestone payments. We assume that 50% (US$270m) of the milestone payments are for the achievement of clinical and regulatory milestones, which we include in our valuation model. We assume that the remaining 50% of the milestones sales-based milestone payments, which we do not include in our valuation model; instead we model a 15% royalty rate. The modelled deal terms are based on relevant benchmarks sourced from EvaluatePharma and a report produced by the industry group BIO. We assume that milestone payments for PXS-6302 are half those for PXS-5505.

Exhibit 8 summarises our key market assumptions for PXS-5505, PXS-6302 and the mannitol business segment. We assume a partner would fund pivotal clinical trials for both drugs. At this stage we include only the MF indication for PXS-5505 and do not include the other pipeline drugs in our valuation model. Our valuation of PXS-6302 is based on use to treat serious burns and to treat keloid scarring resulting from surgical wounds. We do not include its use to reduce the risk of serious scarring after surgery in our valuation model at this time.

With $391m of accumulated losses, we assume that PXS will pay no tax for the foreseeable future.

Exhibit 8: Pharmaxis risk-adjusted DCF valuation and assumptions

Value driver	Success likelihood (%)	rNPV ($m)	rNPV/ share ($)	Assumptions
PXS-5505 in myelofibrosis	15%	81.6	$0.15	Global peak sales of US$420m. We assume prevalence of 15,000 MF patients in the US, 15% penetration; pricing US$100k per patient; global sales double US sales; launch 2027; 15% net royalty.
PXS-6302 in wound scarring	15%	50.0	$0.09	Global peak sales of US$280m. We assume 330,000 cases of keloid scarring in the US each year (0.1% incidence) and 40,000 serious buns; 5% penetration in keloids, 25% in burns; pricing US$3k per patient in keloids and $6k in burns; global sales double US sales; launch 2026; 15% net royalty.
Mannitol business	100%	45.0	$0.08	US Bronchitol sales peak at US$50m in 2027. Rest of World sales grow at 5% p.a. until 2025 then at 3% p.a. Payments to NovaQuest cease after 31 March 2028
SG&A		-16.8	-$0.03	
Portfolio total		**159.9**	**$0.30**	
Cash end FY22e		13.9	$0.03	
Enterprise total		**173.8**	**$0.32**	

Source: Taylor Collison research. Note: We assume addressable markets grow at 3% per year until 2035, after which sales decline by10% p.a.

Strong scientific and management team

Pharmaxis's Board and senior management has the appropriate technical expertise and international pharmaceutical company experience to advance its clinical development programs and grow the mannitol business globally.

Malcolm McComas – Independent Chairman: Mr McComas has been a member of the Board of Directors since July 2003 and Chairman of the Board since 2012. He is a former International Investment Banking Director at Grant Samuel with his tenure spanning from 1999 to 2009. Prior to that, he was Managing Director at NatWest (Citigroup). Mr McComas has led over 50 initial public offerings and significant secondary offerings such as Core Lithium Limited (CXO).

Gary Philips – Chief Executive Officer: Mr Philips was appointed CEO in 2013, having previously been the Chief Operating Officer of Pharmaxis. He has more than 30 years of operational management experience in the pharmaceutical and healthcare industry. Prior to Pharmaxis, Mr Phillips was CEO at Ciba Geigy in Hungary (which merged to form Novartis in 1996) where he was successful in launching a portfolio of new products. In 2001 he joined Novartis Australia as Group Company Head and Chief Executive Officer of its Pharmaceutical Division, successfully launching leading oncology and ophthalmology products

William Delaat – Non-Executive Director: Mr Delaat has been on the Pharmaxis board since 2008. He has over 40 years' experience in the global pharmaceutical industry and was previously a Managing Director of the Australian subsidiary of Merck & Co – a position he held from 1998 until his retirement in 2008. He is the former chair of Medicines Australia and Pharmaceuticals Industry Council.

Neil Graham – Non-Executive Director: Dr Graham was appointed to the Board of Directors in 2020. He is an infectious disease epidemiologist with extensive experience in development of medicines. He is currently CMO at Tiziana Life Sciences and a Non-Executive Director at Aslan Pharmaceuticals Ltd. Previously, Dr Graham was VP and Strategic Program Director of Immunology & Inflammation at Regeneron Inc.

Kathleen Metters – Non-Executive Director: Dr Metters has over 25 years of experience in the discovery and development of novel therapies. She was formerly the Senior Vice President and Head of Worldwide Basic Research for Merck & Co. with oversight of the company's global research projects. In a subsequent role at Merck, she led work on External Discovery and Preclinical Sciences. She is also an independent biopharma consultant and a senior advisor to New York–based Bridge Medicines. Between 1993 and 1997 she was Associate Professor of Epidemiology at John Hopkins University School of Hygiene and Public Health. Dr Metters is a member of the company's Scientific Advisory Board.

David McGarvey – Company Secretary and Chief Financial Officer: Mr McGarvey has been Chief Financial Officer and Company Secretary since December 2002. He has 30 years' experience of building companies from inception into globally successful enterprises. Mr McGarvey has served as CFO at both US Filter and Memtec Limited. He has overseen US listings on the Nasdaq and New York Stock Exchange. Furthermore, Mr McGarvey has managed numerous international mergers and acquisitions. Prior to this, from 1975 to 1985, he held various positions at PWC.

Brett Charlton, PhD – Medical Director: Dr Charlton co-founded Pharmaxis in 1998 and has served continuously as the company's Medical Director, overseeing all aspects of clinical research. He is the author of more than 60 scientific papers, and has over 20 years of experience in clinical trial design and management. He was the founding Medical Director of the National Health Sciences Centre and established its Clinical Trials Unit.

Wolfgang Jarolimek, PhD – Head of Drug Discovery: Dr Jarolimek joined Pharmaxis in 2010 with more than 20 years' experience in pharmaceutical drug discovery and has published more than 30 peer-reviewed articles. He was previously Director of Assay Development and Compound Profiling at the GlaxoSmithKline Centre of Excellence in Drug Discovery in Verona, Italy.

Dieter Hamprecht – Head of Chemistry: Dr Hamprecht has more than 20 years' experience with small molecule and peptide drug discovery. He has contributed to more than 10 drug candidates brought to development and is the coinventor of 50 patent families. He is also the co-author of 30+ scientific publications. Dr Hamprecht was previously Managing Director of Boehringer Ingelheim's research group in Milan and has held senior medicinal chemistry positions at GSK.

Kristen Morgan – Head of Medical and Regulatory Affairs: Ms Morgan has over 20 years' experience in the pharmaceutical industry. She previously held a senior role in Medical Affairs at Sanofi-Aventis and a commercial/sales role at GSK.

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