

Presentation by Chief Executive Officer

pharmaxis

developing breakthrough treatments for fibrosis and inflammation

2022 AGM | 29 November 2022  
Gary Phillips CEO

## Forward looking statement

This document contains forward-looking statements, including statements concerning Pharmaxis' future financial position, plans, and the potential of its products and product candidates, which are based on information and assumptions available to Pharmaxis as of the date of this document. Actual results, performance or achievements could be significantly different from those expressed in, or implied by, these forward-looking statements. All statements, other than statements of historical facts, are forward-looking statements.

These forward-looking statements are not guarantees or predictions of future results, levels of performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this document. For example, despite our efforts there is no certainty that we will be successful in developing or partnering any of the products in our pipeline on commercially acceptable terms, in a timely fashion or at all. Except as required by law we undertake no obligation to update these forward-looking statements as a result of new information, future events or otherwise.

## Pharmaxis Overview



# Executive Summary

- Pharmaxis is a clinical stage drug development company targeting inflammation, fibrosis and selected cancer indications with first in class or best in class small molecule drugs in markets of high value
- Global leader in fibrosis driven by lysyl oxidase enzymes having invested in a multi year research program leveraged with extensive external scientific collaborations
- 5 studies recruiting in 2022 and 2023 that will provide near term value opportunities
- Pro forma cash position at 30 September 2022 of A\$26m<sup>1</sup>, funding the company's clinical programs into early 2024

## Pipeline creates multiple opportunities in high value markets

1. Lead asset PXS-5505 is in a multinational phase 2 trial – a breakthrough clinical program with disease modifying potential in Myelofibrosis. 18 out of 24 targeted patients recruited
2. US investigator led phase 1/2 trial in liver cancer with PXS-5505 as first line treatment added to existing chemotherapy to commence Q4 2022
3. Topical drug PXS-6302 trial in patients with potential to improve function and appearance of established scars. >90% recruited
4. Additional PXS-6302 trial in scar prevention to commence recruitment in 1H 2023
5. Neuro inflammation drug PXS-4728 in phase 2 trial of patients with severe sleep disorder that can lead to neurodegenerative diseases e.g. Parkinson's

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# Shareholders & cash



Financial Information	28 Nov 22
ASX Code	PXS
Share price	\$0.063
Liquidity (turnover last 12 months)	85m shares
Market Cap	A\$40m
Pro forma <sup>1</sup> cash balance (30 September 2022)	A\$26m
Enterprise value	A\$14m
Clinical development program supported by:	
<ul style="list-style-type: none"><li>• R&amp;D tax credits</li><li>• Strategy of partnering deals with pipeline assets</li></ul>	
<ol style="list-style-type: none"><li>1. Proforma cash includes cash of \$12m, estimated 2022 R&amp;D tax credit of \$5m (expected receipt H2 CY22), and capital raising of \$10m less offer costs</li></ol>	

Institutional Ownership	27 October 22
BVF Partners LP	17%
Karst Peak Capital Limited	11%
D&A Income Limited	7%
Regal Funds Management Pty Ltd	6%
Platinum Investment Management Limited	5%
<b>Total Institutional Ownership</b>	<b>~46%</b>

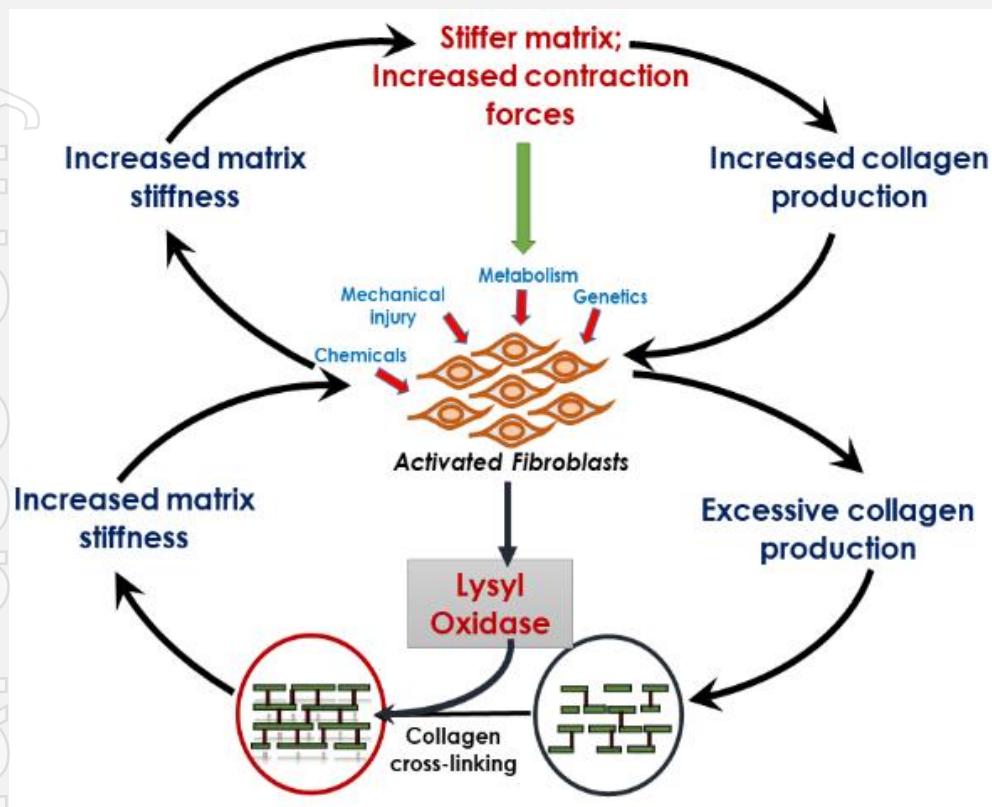
## Share Price



# Pharmaxis is the global leader in lysyl oxidase chemistry and biology

Multi year research program leveraged with extensive scientific collaborations worldwide has delivered 2 drugs in the clinic

## Lysyl oxidases are the final stage in fibrosis



Tissue stiffening due to increases in collagen and number of cross-links which is a hallmark of fibrosis, is preventable through lysyl oxidase inhibition; at the heart of a true anti-fibrotic therapy

### ■ PXS-5505

- Oral dosage form – four capsules twice a day
- Patent filed - priority date 2018
- Strong pre clinical evidence in models of fibrosis and cancer
- INDs approved for myelofibrosis and hepatocellular carcinoma
- Potential in multiple cancer indications
- Phase 1 data demonstrates a safe, well tolerated drug that gives >90% inhibition of LOX enzymes

### ■ PXS-6302

- Topical dosage form
- Patent filed - priority date 2019
- Strong pre clinical evidence in models of skin fibrosis and scarring
- Potential in prevention of scar formation and modification of existing scars
- Phase 1a (healthy volunteer) data demonstrates a safe, well tolerated drug that gives full inhibition of LOX enzymes in the skin with minimal systemic exposure

## Program Update



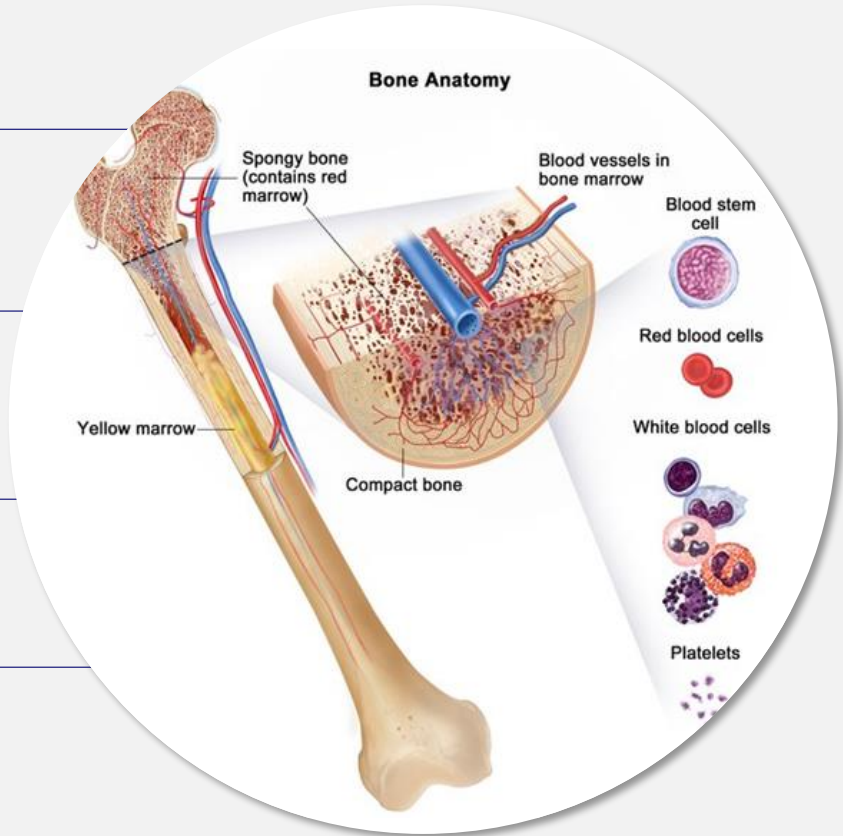


# Myelofibrosis

A rare type of bone marrow cancer that disrupts the body's normal production of blood cells

## KEY FACTS

- Affects ~15 in 1m people worldwide
- 5 Years Median survival
- Age of onset typically from age 50
- 11% transformation to leukemia



**Primary Myelofibrosis** is caused by a build up of scar tissue (fibrosis) in bone marrow reducing the production of blood cells:

- Reduced red blood cells can cause extreme tiredness (fatigue) or shortness of breath
- Reduced white blood cells can lead to an increased number of infections
- Reduced platelets can promote bleeding and/or bruising
- Spleen increases blood cell production and becomes enlarged
- Other common symptoms include fever, night sweats, and bone pain

## Current Standard of Care; JAK inhibition

- Symptomatic relief plus some limited survival improvement. 75% discontinuation at 5 years
- Median overall survival is 14 – 16 months after discontinuation

## Commercial Opportunity

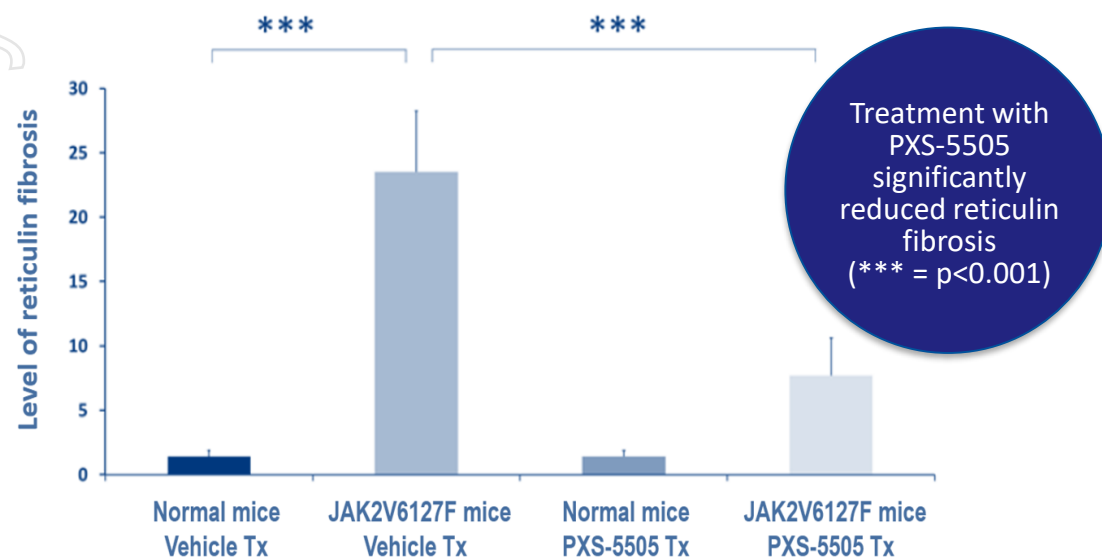
- Current standard of care ; revenue ~US\$1b per annum



## Myelofibrosis - PXS-5505; an effective and safe inhibitor of LOX in myelofibrosis patients

Pre clinical and clinical studies strongly support entry into long term phase 2 patient studies

### PXS-5505 attenuates hallmarks of primary myelofibrosis in mice<sup>3</sup>

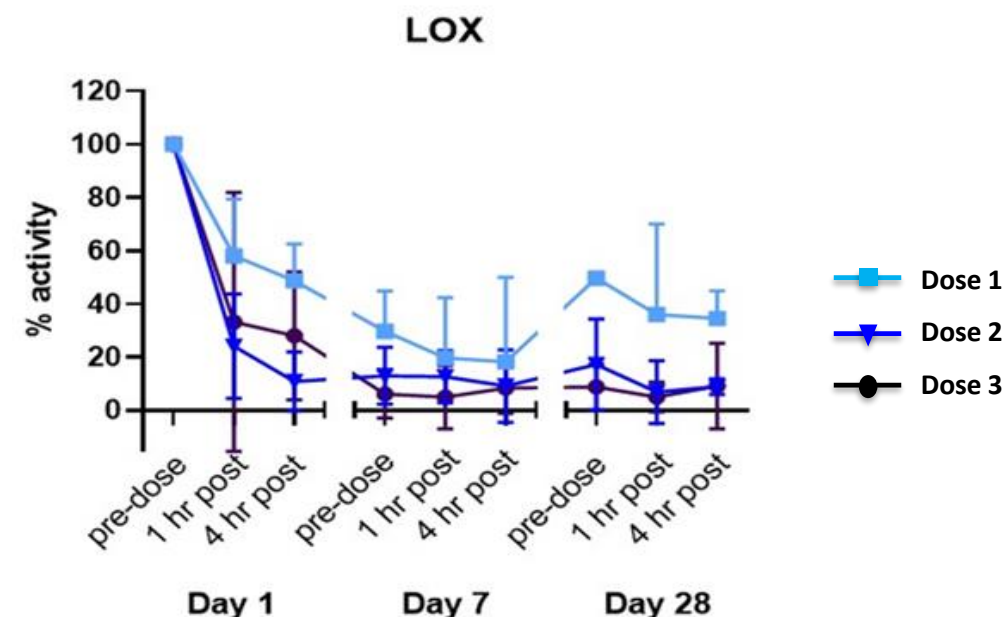


*"None of the drugs approved to date consistently or meaningfully alter the fibrosis that defines this disease. PXS-5505 has a novel mechanism of action by fully inhibiting all LOX enzymes.*

*Preliminary data thus far, demonstrate that PXS-5505 leads to a dramatic, >90% inhibition of LOX and LOXL2 at one week and 28 days. This confirms what's been shown in healthy controls as well as mouse models, that this drug can inhibit the LOX enzymes in patients. Inhibiting these enzymes is a novel approach to the treatment of myelofibrosis by preventing the deposition of fibrosis and ultimately reversing the fibrosis that characterizes this disease"*

Dr Gabriela Hobbs<sup>1</sup>

### PXS-5505 – Phase 1c dose escalation in MF patients



- Open label dose escalation in JAK-inhibitor unsuitable<sup>2</sup> primary MF or post-ET/PV MF patients
- Maximum of 3 patients on each dose for 28 days
- Good safety profile with no adverse events at highest dose
- >90% inhibition of LOX and LOXL2 at trough on highest dose at day 7 and 28

<sup>1</sup> Assistant Professor, Medicine, Harvard Medical School & Clinical Director, Leukaemia, Massachusetts General Hospital

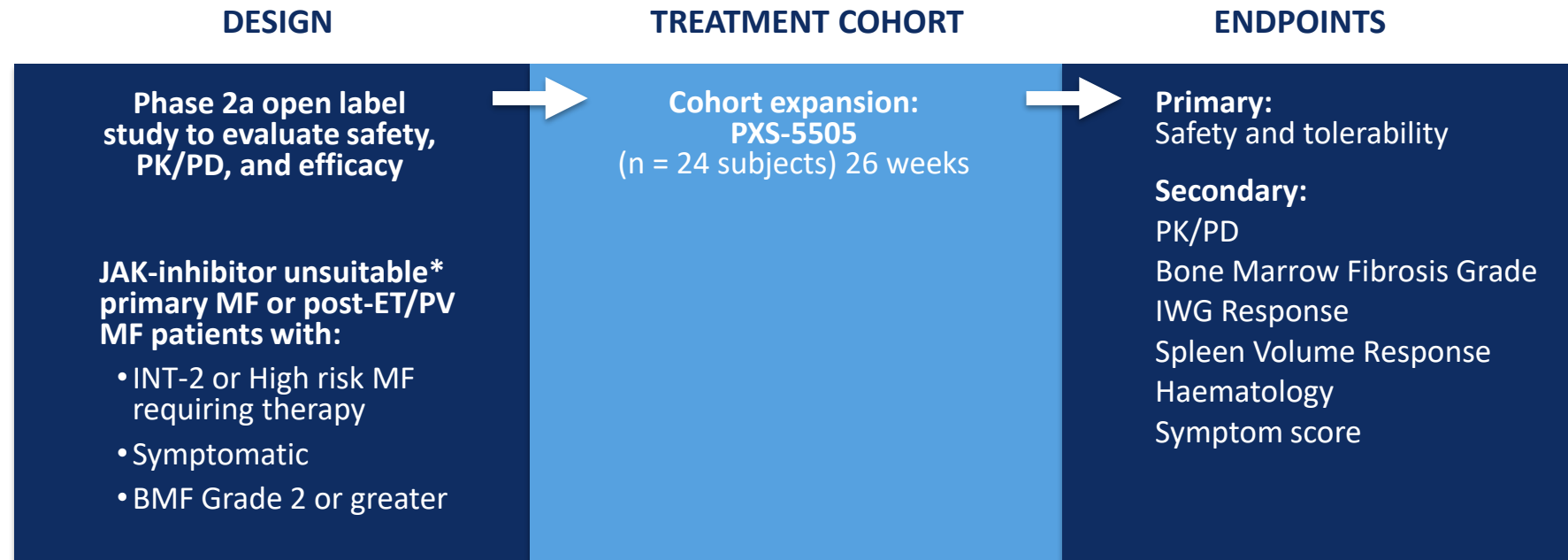
<sup>2</sup> Unsuitable = ineligible for JAKi treatment, intolerant of JAKi treatment, relapsed during JAKi treatment, or refractory to JAKi treatment. JAKi – Janus Kinase inhibitor, MF myelofibrosis, ET Essential Thrombocythaemia, PV polycythaemia vera

<sup>3</sup> Ref Graph1: Leiva et al. Intl J Hemat 2019. <https://doi.org/10.1007/s12185-019-02751-6>

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# Myelofibrosis – PXS-5505 Phase 1/2a Trial

6 month monotherapy study with meaningful safety and efficacy endpoints



FDA granted orphan drug designation July 2020 and IND approved August 2020

20 sites across 4 countries (Australia, South Korea, Taiwan, USA)

Study budget to spend ~A\$6.2m

Study recruitment commenced Q4 2021, study targeted to report mid 2023

# Myelofibrosis – PXS-5505 Phase 2a Trial (*INTERIM DATA*)

Very well tolerated with encouraging signs of clinical efficacy in JAK inhibitor unsuitable patients

DESIGN	TREATMENT COHORT	ENDPOINTS
<p>Phase 2a open label study to evaluate safety, PK/PD, and efficacy</p> <p><b>JAK-inhibitor unsuitable* primary MF or post-ET/PV MF patients with:</b></p> <ul style="list-style-type: none"><li>• INT-2 or High risk MF requiring therapy</li><li>• Symptomatic</li><li>• BMF Grade 2 or greater</li><li>• Median survival after JAK-inhibitor discontinuation; approximately 1 year</li></ul>	<p>Cohort expansion: PXS-5505 (n = 24 subjects) 26 weeks</p> <ul style="list-style-type: none"><li>• A total of 18 patients have been enrolled</li><li>• 6 patients having completed 24 weeks of treatment.</li><li>• 4 patients have dropped out of the study due to a lack of clinical response.</li></ul>	<p><b>Primary:</b></p> <p>PXS5505 has been well tolerated with no serious treatment related adverse events reported.</p> <p><b>Secondary:</b></p> <ul style="list-style-type: none"><li>• 2/6 patients show clinically important improvement in symptoms.</li><li>• 5/6 patients show either stable or improved bone marrow fibrosis scores of <math>\geq 1</math> grade.</li><li>• 5/6 have stable or improved platelet and/or haemoglobin scores</li><li>• No reductions were seen in spleen volume</li></ul>



*“PXS-5505 continues to be very well tolerated in the clinic with no serious treatment related adverse events reported.*

*Though still early in the dose expansion phase of the study, PXS5505 appears to be stabilising and in some cases, improving the hemoglobin and platelet counts, which has also been associated with symptom improvements in those patients that were treated to 24 weeks.*

*This is encouraging given the poor prognosis seen after ruxolitinib discontinuation with a median overall survival of only 11-14 months typical of this study population. These results support further clinical investigation of PXS5505 in myelofibrosis.”*

Dr Gabriela Hobbs MD,  
Assistant Professor, Medicine, Harvard  
Medical School & Clinical Director,  
Leukemia Service, Massachusetts General  
Hospital

\*Unsuitable = ineligible for JAKi treatment, intolerant of JAKi treatment, relapsed during JAKi treatment, or refractory to JAKi treatment. JAKi – Janus Kinase inhibitor, MF myelofibrosis, ET Essential Thrombocythaemia, PV polycythaemia vera, INT intermediate,

BMF bone marrow fibrosis, PK pharmacokinetics, PD pharmacodynamics, IWG International Working Group Myeloproliferative Neoplasms

# Hypertrophic and keloid scarring

Cutaneous scarring following skin trauma or a wound is a major cause of morbidity and disfigurement

## KEY FACTS

- 100m patients develop scars in the developed world alone each year as a result of elective operations and operations after trauma

- Hypertrophic scars and keloids are fibroproliferative disorders that may arise after any deep cutaneous injury caused by trauma, burns, surgery, etc.

- Hypertrophic scars and keloids are cosmetically and functionally problematic significantly affecting patients' quality of life



"In (preclinical) models of scarring we found that topical application of PXS-6302 reduces collagen deposition and cross-linking and improves scar appearance without reducing tissue strength. This is a unique way of modulating a critical stage in scar formation and maintenance and holds out great promise for the treatment of scars."  
- Dr Mark Fear,  
UWA

- Mechanisms underlying scar formation are not well established; prophylactic and treatment strategies remain unsatisfactory

- Current standard of care includes:

- Corticosteroids
- Surgical revision
- Cryotherapy
- Laser therapy
- 5-fluorouracil



- Pre clinical evidence

- Treatment with PXS-6302 monotherapy demonstrates cosmetic and functional improvements to scarring in pre clinical models<sup>1</sup>

- Clinical evidence

- 1 month phase 1a in healthy volunteers demonstrates good tolerability and full inhibition of LOX in skin.

- Commercial Opportunity

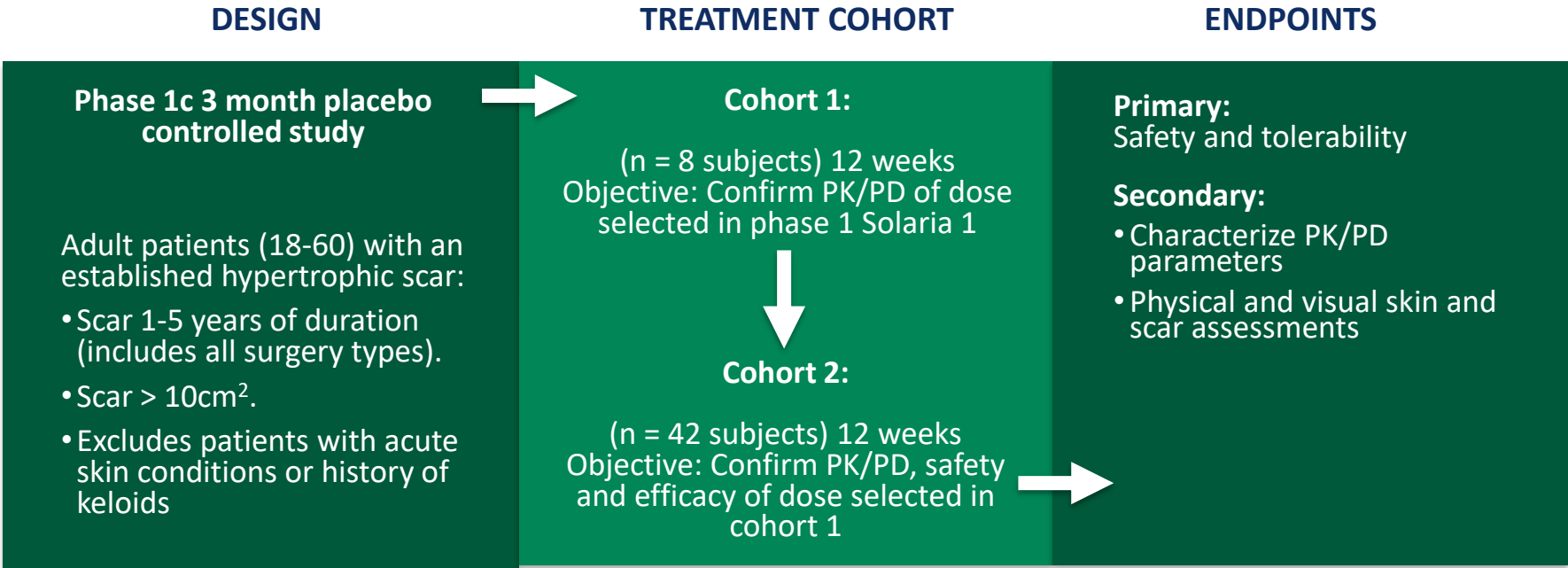
- Total scar treatment market in 2019 exceeded US\$19b. Keloid and hypertrophic scar segment ~US\$3.5b

Note 1: Chaudhari et al, Topical application of an irreversible small molecule inhibitor of lysyl oxidases ameliorates skin scarring and fibrosis, Nature communications 2022  
<https://doi.org/10.1038/s41467-022-33148-5>

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# Established Hypertrophic Scarring – PXS-6302 Phase 1c Trial (Solaria 2)

3 month monotherapy study to assess dosage, tolerability and efficacy endpoints



Investigator initiated study (sponsor UWA) - long term collaboration with UWA to research and develop PXS-6302 supported by Australian NHMRC grants

Single site study in Perth Australia

Study budget to spend; A\$0.3m

Study recruitment commenced Q1 2022, study targeted to report H1 2023

\* PK pharmacokinetics, PD pharmacodynamics,



Established Hypertrophic Scarring – PXS-6302 Phase 1c Trial (Solaria 2)

3 month monotherapy study to assess dosage, tolerability and efficacy endpoints

DESIGN	TREATMENT COHORT	ENDPOINTS
<p><b>Phase 1c 3-month placebo controlled study</b></p> <p>Adult patients (18-60) with an established hypertrophic scar:</p> <ul style="list-style-type: none"><li>• Scar 1-5 years of duration (includes all surgery types).</li><li>• Scar &gt; 10cm<sup>2</sup>.</li><li>• Excludes patients with acute skin conditions or history of keloids</li></ul>	<p><b>Cohort 1:</b></p> <p>Fully recruited</p> <p><b>Cohort 2:</b></p> <ul style="list-style-type: none"><li>• A total of 38 out of 42 patients have been enrolled</li><li>• Dosage regimen modified to reduce drug exposure but still maintain the overall high level of enzyme inhibition.</li></ul>	<p><b>Cohort 1:</b></p> <ul style="list-style-type: none"><li>• Skin biopsies show skin penetration and high inhibition of LOX</li><li>• Reduction in biomarkers of the scarring process suggests a disease modifying effect.</li><li>• Clinician notes positive changes in appearance and pliability</li><li>• Four patients withdrew after experiencing redness &amp; itchiness at the site of application that resolved on treatment cessation and informed the decision to reduce dosage frequency for Cohort 2</li></ul>

“We have noted positive changes in appearance and pliability of scars in those patients on active drug that now need to be confirmed by the results from the placebo controlled phase of this trial later this year.

We are learning a lot as we move from the promising pre-clinical work done at UWA and into the clinic where we have many patients who are in great need of a treatment that can improve both the cosmetic appearance of their scars and improve the functionality of their scarred skin; factors that have a huge impact on patient’s wellbeing.”

Professor Fiona Wood  
Burns Service of Western Australia  
Director of the Burn Injury Research Unit  
University of Western Australia

\* PK pharmacokinetics, PD pharmacodynamics,

## Upcoming News Flow





## Five trials to deliver near term value

Pipeline creates multiple opportunities in high value markets

	Indication	Addressable market (US\$)	Trial design	# patients	Status	Data
PXS-5505	Myelofibrosis (MF)	\$1 billion	Phase 2 open label 6 month study in JAK intolerant / ineligible myelofibrosis patients	24	Recruiting	Interim data released Full data mid 2023
	Hepatocellular Carcinoma (HCC)	\$7 billion	Phase 1c open label dose escalation study in newly diagnosed patients with unresectable HCC on top of standard of care (PD-L1 inhibitor + anti VEGF)	18	First Patient Q4 2022	H1 2024
PXS-6302	Modification of established scars	\$3.5 billion	Phase 1c 3 month placebo controlled study in patients with established scars (>1 year old)	50	Recruiting	H1 2023
	Scar prevention post surgery	\$3.5 billion	Phase 1c 3 month placebo controlled study in patients with scarring subsequent to a burns injury	50	First patient H1 2023	H1 2024
PXS-4728	Isolated REM sleep behaviours disorder (iRDB) and neuro inflammation	\$3.5 billion	Phase 2 double blind, placebo controlled study in patients with iRBD	40	First patient H1 2023	H1 2025

# News flow

Q4 2022 and H1 2023 anticipated news flow

***Strong and growing pipeline with advancement in studies expected to provide value inflection points in FY23***



## Q4 2022

- PXS-5505 phase 1c liver cancer (HCC) study – starts recruitment
- PXS-5505 phase 2a myelofibrosis study – fully recruited
- PXS-5505 publications by KOL's in other cancers
- Two presentations at ASH (American Society of Haematology) conference in November
  - PXS-5505 phase 1c/2 study in myelofibrosis
  - PXS-5505 pre-clinical data in Myeloid Neoplasms e.g. myelodysplastic syndrome



## Q1 2023

- LOX topical drug PXS-6302 commences independent investigator patient studies – scar prevention
- LOX topical drug PXS-6302 top line data from established scars study
- PXS-5505 publications by KOL's in other cancers



## Q2 2023

- PXS-5505 phase 2a myelofibrosis study completed and reports safety and efficacy data
- PXS-4728 iRBD / neuro inflammation study commences recruitment



## Financial Overview

**pharmaxis**

developing breakthrough treatments for fibrosis and inflammation

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David McGarvey CFO

# Financials

## Income statement highlights

Periods ended (A\$'000)	Three months		Twelve months		
	Sep-22	Sep-21	Jun-22	Jun-21	Jun-20
<b>Segment Financials</b>					
<b>New drug development</b>					
Oral LOX (external costs)	(1,009)	(1,467)	(5,431)	(2,521)	(3,124)
Other program external costs (net of grants)	(300)	(303)	(1,712)	(1,850)	(3,315)
Employee costs	(891)	(715)	(2,943)	(3,270)	(3,373)
Overhead	(161)	(102)	(374)	(396)	(460)
R&D tax credit and other income	-	-	5,600	148	5,159
EBITDA	(2,361)	(2,587)	(4,859)	(7,889)	(5,113)
<b>Mannitol respiratory business</b>					
Sales	760	3,272	7,427	6,680	7,027
Other revenue and income	7,192	2,342	2,342	15,986	20
	7,952	5,614	9,769	22,666	7,047
Expenses – employee costs	(1,119)	(1,197)	(4,760)	(5,558)	(5,855)
Expenses – manufacturing purchases	(648)	(1,205)	(2,729)	(1,168)	(1,456)
Expenses – other	(806)	(1,142)	(3,584)	(4,483)	(3,713)
EBITDA	5,379	2,070	(1,304)	11,457	(3,977)
<b>Corporate – EBITDA</b>	(333)	(678)	(4,080)	(3,793)	(2,990)
<b>Total Adjusted EBITDA</b>	2,685	(1,195)	(10,243)	(225)	(12,080)
<b>Net profit (loss)</b>	943	(3,029)	(1,934)	(2,970)	(13,943)

# Financials

## Cash

Periods ended (A\$'000)	Three months		Twelve months		
	Sep-22	Sep-21	Jun-22	Jun-21	Jun-20
<b>Cash</b>					
Cash at period end	11,597	18,712	11,597	18,712	14,764
Cash received/receivable post period end					
2022 R&D tax credit - expected H2 CF 2022	4,900				
Placement (\$5.1m subject to shareholder approval)	9,235				
Proforma cash at period end	25,732				

## Cash Flow Statement Highlights

### Operations

Receipts from customers	404	1,498	8,313	7,242	7,775
R&D tax incentive	-	-	-	5,048	6,271
Milestone payments	-	-	-	13,844	-
Sale of Orbital/distribution rights	7,192	2,340	2,902	1,365	-
Other	17	17	1,005	236	-
Payments to suppliers, employees etc (net)	(4,951)	(5,757)	(28,322)	(24,663)	(27,330)
Total operations	2,662	(1,902)	(16,102)	3,072	(13,284)
Investing (capex & patents)	(26)	(40)	(306)	(644)	(574)
Finance lease payments <sup>1</sup>	(545)	(596)	(2,379)	(2,305)	(2,232)
Financing agreement payments <sup>2</sup>	(14)	(43)	(62)	(240)	270
Share issue - net	-	-	9,074	4,065	-
Net increase (decrease) in cash	2,660	(2,581)	(9,775)	3,948	(16,360)

1. Lease over 20 Rodborough Rd (to May 2024) – total liability at 30 June 2022: \$4.4 million
2. NovaQuest financing – not repayable other than as % of US Bronchitol revenue through to March 2028