

pharmaxis

Investor Presentation | October 2022 Gary Phillips CEO

developing breakthrough treatments for fibrosis and inflammation

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# Key Highlights

**Phase 2a Myelofibrosis** 

**PXS-5505 Interim Data** from 6 patients has shown encouraging signs of clinical efficacy and

excellent safety profile

**Interim Data from 8** patients treated with PXS-6302 shows a high level of inhibition of enzymes and changes in biomarkers that are implicated in scarring



Three novel drugs across five indications with multiple key catalysts over the next 6-9 months



**Corporate strategy** delivering non-dilutive cash to fund development of clinical pipeline



**Experienced Scientific Management Team -**Significant global experience in drug development, commercialisation and partnering



Pro forma cash position of A\$30.0m<sup>1</sup>, funding the company's clinical programs into early 2024





# 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
  - Undertaking a capital raising of approximately A\$10 million via a two-tranche placement at \$0.06 per share
    - Funding from the capital raising will be used towards the company's current clinical programs in Myelofibrosis, Scarring, Liver Cancer and Parkinson's disease and provide general working capital

## Pipeline creates multiple opportunities in high value markets

- Lead asset PXS-5505 is in a multinational phase 2 trial a
  breakthrough clinical program with disease modifying potential in
  Myelofibrosis. 15 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. >60% 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



## 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 Stiffer matrix; Increased contraction forces Increased matrix Increased collagen stiffness production Activated Fibroblasts Increased matrix **Excessive collagen** stiffness production Lysyl Oxidase Collagen cross-linking

Tissue stiffening due to increases in collagen and number of crosslinks 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





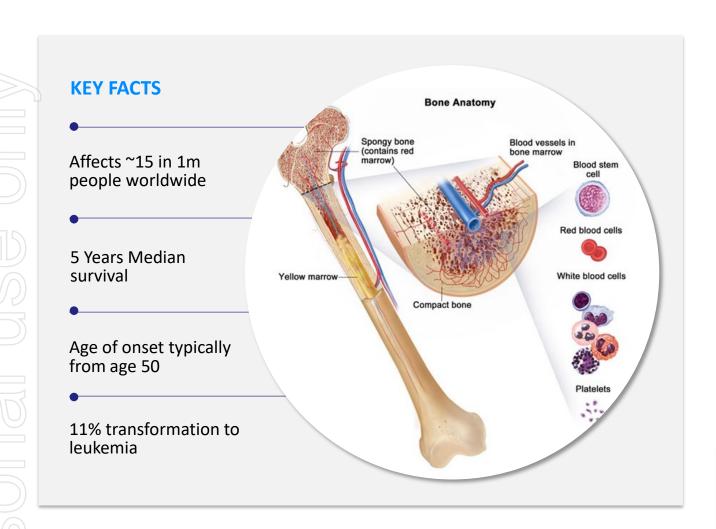
# Program Update





# Myelofibrosis

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



**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**

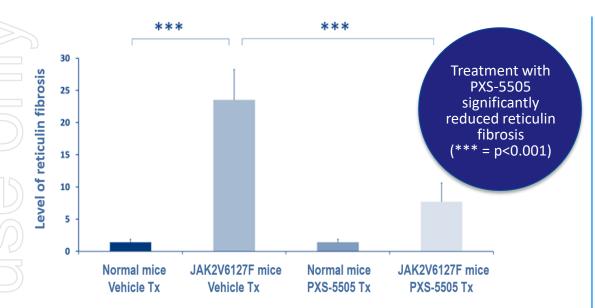
 Current standard of care; revenue ~US\$1b per annum

## **Program Update**

# 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>

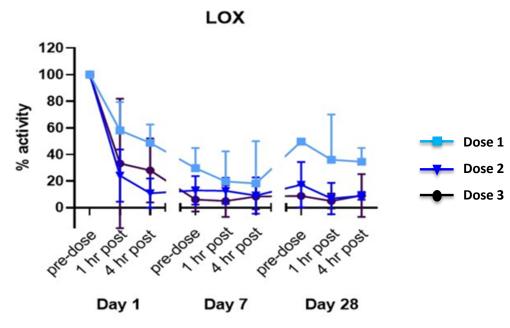


"None of the drugs approved to date consistently or meaningfully alter the fibrosis that defines this disease. PXS-5505 has a novel mechanism of action by fully inhibiting all LOX enzymes.

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

<sup>&</sup>lt;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

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

6 month monotherapy study with meaningful safety and efficacy endpoints

#### **DESIGN** TREATMENT COHORT **ENDPOINTS** Phase 2a open label **Cohort expansion: Primary:** study to evaluate safety, Safety and tolerability PXS-5505 PK/PD, and efficacy (n = 24 subjects) 26 weeks **Secondary:** PK/PD JAK-inhibitor unsuitable\* Bone Marrow Fibrosis Grade primary MF or post-ET/PV **IWG** Response MF patients with: Spleen Volume Response • INT-2 or High risk MF Haematology requiring therapy Symptom score Symptomatic • BMF Grade 2 or greater

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\$7.5m

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

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# 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**

Phase 2a open label study to evaluate safety, PK/PD, and efficacy

JAK-inhibitor unsuitable\* primary MF or post-ET/PV MF patients with:

- INT-2 or High risk MF requiring therapy
- Symptomatic
- BMF Grade 2 or greater
- Median survival after JAKinhibitor discontinuation; approximately 1 year

Cohort expansion:
PXS-5505
(n = 24 subjects) 26 weeks

- A total of 15 patients have been enrolled
- 6 patients having completed
   24 weeks of treatment.
- 4 patients have dropped out of the study due to due to a lack of clinical response.

## **Primary:**

PXS5505 has been well tolerated with no serious treatment related adverse events reported.

## **Secondary:**

- 2/6 patients show clinically important improvement in symptoms.
- 5/6 patients show either stable or improved bone marrow fibrosis scores of ≥1 grade.
- 5/6 have stable or improved platelet and/or haemoglobin scores
- No reductions were seen in spleen volume

"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

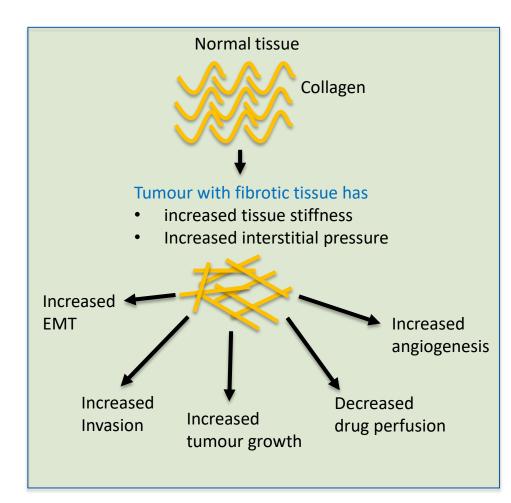


## **Program Update**

# Hepatocellular Carcinoma (HCC)

4th leading cause of cancer-related mortality worldwide with a 19.6% 5-year relative survival

- Primary liver malignancies have doubled in incidence over the last two decades.
- e 4th leading cause of cancerrelated mortality worldwide with a 19.6% 5-year relative survival
- Accumulation of collagen cross-links increases stromal stiffening and interstitial fluid pressure reducing delivery of chemotherapy and immunotherapy
- Current standard of care
   20-30% are resectable at presentation with many patients relying on systemic therapy:
  - Tyrosine kinase inhibitors
    PD-L1 inhibitors + anti-VEGF



- Pre-clinical data (Rochester Uni; Aug 2021)
  - Tumour tissue specimens show LOX enzymes are significantly elevated in human liver cancer and correlate with poor prognosis.
  - PXS-5505 with or without chemotherapy treatment in a preclinical model significantly improves survival, delays tumour growth, and reduces intratumoral pressure.

## **Commercial Opportunity**

Drugs market currently worth ~US\$2bn with rising incidence forecasted to drive growth to ~US\$7bn by 2027

# Hepatocellular carcinoma - PXS-5505 Phase 1b/2a Trial

First line combination treatment with standard of care to assess safety and efficacy endpoints

#### **DESIGN** TREATMENT COHORT **ENDPOINTS** Open label phase 1b/2a of Phase 1b: **Primary:** PXS-5505 combined with Dose escalation design Maximum tolerated dose atezolizumab (PD-L1 3 dose levels antibody) and bevacizumab **Secondary:** n = 12-18 subjects (anti-VEGF antibody) 12 weeks Objective response rate (RECIST 1.1) in evaluable Newly diagnosed patients after completing at hepatocellular carcinoma least 4 cycles of treatment (3 months). Adult patients Phase 2a: Progression free survival Systemic therapy naïve Dose selected from phase 1b $n = ^40$ subjects Overall survival • Unresectable or metastatic ~26 weeks

IND (University of Rochester) reviewed by FDA November 2021

Phase 1b trial being conducted by Rochester Medical Centre, New York State, USA (Study sponsor).

Opened for enrollment 23 Sept

Phase 1b study budget to spend ~A\$1.7m

Study recruitment to commence Q4 2022, study targeted to conclude H1 2024

https://clinicaltrials.gov/ct2/show/NCT05109052



# 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 crosslinking 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.

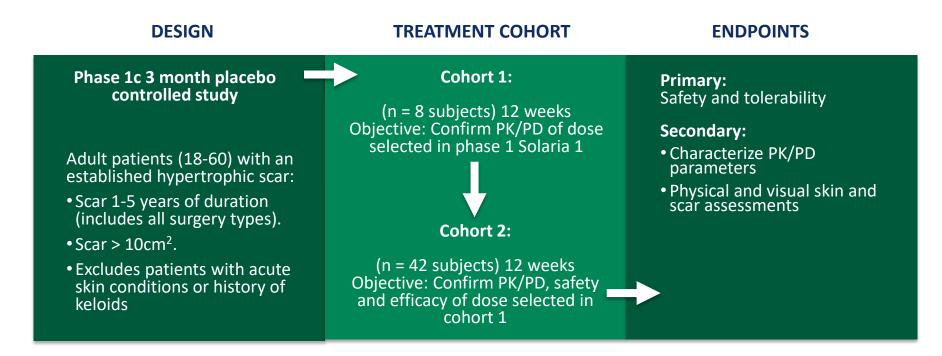
## Commercial Opportunity

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



## 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



## 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**

# Phase 1c 3-month placebo controlled study

Adult patients (18-60) with an established hypertrophic scar:

- Scar 1-5 years of duration (includes all surgery types).
- Scar  $> 10 \text{cm}^2$ .
- Excludes patients with acute skin conditions or history of keloids

#### Cohort 1:



Fully recruited

#### Cohort 2:

- A total of 24 out of 42 patients have been enrolled
- Dosage regimen modified to reduce drug exposure but still maintain the overall high level of enzyme inhibition.

#### Cohort 1:

- Skin biopsies show skin penetration and high inhibition of LOX
- Reduction in biomarkers of the scarring process suggests a disease modifying effect.
- Four patients withdrew after experiencing redness & itchiness at the site of application that resolved on treatment cessation and informed the decision to reduce dosage frequency for Cohort 2

"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

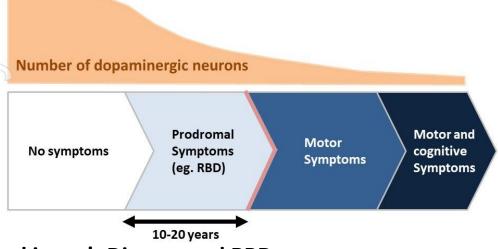
Burns Service of Western Australia Director of the Burn Injury Research Unit University of Western Australia



## **Program Update**

## iRBD & Neuro Inflammation - Using a sleep disorder to target Parkinson's Disease

SSAO inhibition proven effective mechanism against neuro inflammation and is neuro protective in pre clinical models

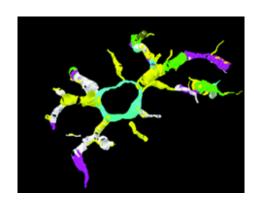


## Parkinson's Disease and RBD

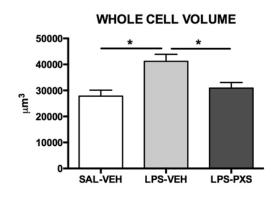
- More than 50% of dopaminergic neurons in the substantia nigra are lost at the onset of motor symptoms in Parkinson's Disease.
- Prodromal symptoms, such as isolating REM sleep behavior disorder (iRBD), proceed the onset of motor cognitive dysfunction by 10-20 years.
- 70% of iRBD patients transition to a neurodegenerative disease such as Parkinson's disease and Dementia with Lewy Bodies

## PXS-4728 and neuro inflammation

- PXS-4728 has already undergone extensive development by Boehringer Ingelheim
- PXS-4728 inhibits SSAO and MAOB in the brain both of which play a role in neurodegenerative diseases such as Parkinson's.
- Dual SSAO & MAO-B inhibition protects against neuronal degradation in pre clinical models<sup>2</sup>
- MAO-B inhibition alone (selegiline) does not offer any protection in the same model<sup>2</sup>



Activated microglia - reconstruction



Change in Microglia whole cell volume in the Substantia Nigra (SN) after LPS<sup>1</sup>



<sup>1.</sup> Becchi et al. Semicarbazide Sensitive Amine Oxidase/Vascular Adhesion Protein-1 inhibition reduces lipopolysaccharide-induced neuroinflammation *Br. J. Pharmacol*; DOI:10.1111/bph.13832

## iRDB and Neuro Inflammation - Parkinson's UK Funding

PXS-4728 to proceed to phase 2 trial

## **Short and longer term commercial opportunities**

- Current standard of care for iRBD is melatonin. There remains a high unmet need.
- >8% of 70 89 year olds have iRBD
- >70 % of iRBD patients develop Parkinson's disease and the related  $\alpha$ -synuclein deposition disorders, dementia with Lewy bodies (DLB) and multiple system atrophy (MSA).
- Parkinson's market ~3.5bn in 2019

## **Clinical Trial**

- 40 patients
- Randomised, double blind, placebo controlled clinical trial with iRBD
- 12 weeks of treatment with oral PXS-4728
- Two sites University of Sydney and the University of Oxford
- Expected to commence dosing in H1 2023
- Efficacy endpoints for iRBD and neuroinflammation

## **Parkinson's UK Funding Agreement**

## Clinical trial in precursor to Parkinson's Disease

- The funding agreement with Parkinson's UK entails up to £2.9m (~A\$4.9m) to be paid to Pharmaxis to run the phase 2 trial with advance payments received as the trial progresses.
- Pharmaxis is providing the study drug and the compound that will be used to measure inflammation in the brain scan of trial participants. The total is expected to cost approximately A\$5.8 million.
- Parkinson's UK will receive a return of up to 4 times their funding from royalties on future revenue Pharmaxis receives from commercialising PXS-4728 in neurological diseases and up to 2 times in other indications.



# Mannitol respiratory business (Bronchitol® and Aridol®)

Sales growth expected from Bronchitol sales in US and Russia

## **Sales**

- Bronchitol > 75% of sales
- Strong short term growth from Russia
- Sales growth expected in approved markets as patients access hospitals again post COVID-19 restrictions
- Strong longer term growth contribution expected from US

## **Expenses**

Relatively fixed production cost base

## **Segment EBITDA**

- Negative EBITDA for FY 2022 \$1.3m
- Forecast positive EBITDA as CF clinics reopen post COVID
- US volumes contribute to mannitol segment generating profit



## **Bronchitol in US**

 US CF market >65% of global market in value

US market doubles global cystic fibrosis patient opportunity with attractive pricing

- US sales commenced in Q1 CY 2021

   delay in patient initiation due to
   COVID
- High teens % of Chiesi sales + supply contract - ~20% of Chiesi US Bronchitol net sales flow directly to the Pharmaxis bottom line



# 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
	PXS	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
	302	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
	PXS-6302	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

## **Upcoming News Flow**

## 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 2a myelofibrosis study interim data
- 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



## Details of the Offer

Pharmaxis is undertaking a capital raising of approximately A\$10 million, funding the company's clinical programs into early 2024

Offer Structure and Size	<ul> <li>A two tranche placement to institutional, sophisticated and professional investors of A\$10m, comprising:</li> <li>Tranche 1 – placement of approximately A\$4.9m under the company's existing 15% Placement capacity under ASX Listing Rule 7.1 ("Tranche 1"); and</li> <li>Tranche 2 – placement of approximately A\$5.1m subject to shareholder approval at the AGM to be held on 29 November 2022 ("Conditional Placement");</li> </ul>
Offer Price	<ul> <li>Offer Price of \$0.06 per share represents a:</li> <li>23.1% discount to the last close of \$0.078 on Monday, 17 October 2022;</li> <li>24.8% discount to the 5-day VWAP of \$0.080</li> </ul>
Use of Funds	<ul> <li>Funding from the capital raising will be used towards the Company's current clinical study in myelofibrosis as well as other clinical studies in scarring, liver cancer and Parkinson's disease, and provide working capital</li> </ul>
Ranking	Shares issued under the Offer will rank pari passu with existing Shares on issue
Joint Lead Managers	Morgans Corporate Limited and Bell Potter Securities Limited are Joint Lead Managers to the Offer

## Indicative Timetable

## Indicative capital raising timetable

Trading halt		Tuesday, 18 October 2022
Capital raising announced and trading halt lifted –	Shares recommence trading on ASX	Wednesday, 19 October 2022
Settlement of first tranche Placement		Tuesday, 25 October 2022
Allotment and commencement of trading of New S	hares issued under the Placement	Wednesday, 26 October 2022
Approval of Conditional Placement at AGM		Tuesday, 29 November 2022
Settlement of Conditional Placement <sup>1</sup>		Friday, 2 December 2022
Allotment, quotation and trading of New Shares is:	sued under the Conditional Placement <sup>1</sup>	Monday, 5 December 2022

<sup>1</sup>Subject to approval at the AGM

The timetable above is indicative only and may be varied by the subject to the ASX Listing Rules



## Capital Structure

**Pharmaxis Capital Structure** 

Institutional Ownership	30 June 22
BVF Partners LP	18.7%
Karst Peak Capital Limited	12.4%
D&A Income Limited	7.4%
Total Institutional Ownership	40.0%

Capital Structure (17 October 2022)	\$m
ASX Code	PXS
Share price	\$0.078
Liquidity (turnover last 12 months)	100m shares
Market Cap	A\$42.8m
Pro forma cash balance (Including capital raising) 1,2	A\$30.0m

Clinical development program supported by:

- R&D tax credits
- Strategy of partnering deals with pipeline assets
- Proforma cash includes cash of \$9m, estimated 2022 R&D tax credit of \$5 million (expected receipt H2 CY22), and Aptar option exercise fee A\$7m received August 2022
- Based on June 2022 pro forma cash position of \$20.87 million and capital raising of \$10.0 million less offer costs

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## Board

## Significant international pharmaceutical experience



#### Malcolm McComas - Chair

- Former investment banker and commercial lawyer
- Former MD Citi Group
- Has worked with many high growth companies across various industry sectors and has experience in equity and debt finance, acquisitions and divestments and privatisations
- Joined Pharmaxis Board in 2003
- Chair since 2012



## **Gary Phillips – Chief Executive Officer**

- 30+ years' of operational management experience in the pharmaceutical and healthcare industry in Europe, Asia and Australia
- Joined Pharmaxis in 2003 and was appointed Chief Executive Officer in March 2013 at which time he was Chief Operating Officer
- Previously held country and regional management roles at Novartis Hungary, Asia Pacific and Australia



#### Dr Kathleen Metters - Non-Executive Director

- Former Senior Vice President and Head of Worldwide Basic Research for Merck & Co. with oversight of all the company's global research projects
- In a subsequent role at Merck &Co she led work on External Discovery and Preclinical Sciences
- Former CEO of biopharmaceutical company Lycera Corp



#### Dr Neil Graham - Non-Executive Director

- Former VP of immunology and inflammation responsible for strategic program direction overseeing pipeline development and clinical programs at Regeneron (REGN:US)
- Former SVP program and portfolio management at Vertex Pharmaceuticals
- Former Chief Medical Officer at Trimeris Inc and Tibotec Pharmaceuticals

# Experienced senior management team

Significant global experience in drug development, commercialisation and partnering



## **Gary Phillips – CEO and Managing Director**

- 30+ years' of operational management experience in the pharmaceutical and healthcare industry in Europe, Asia and Australia
- joined Pharmaxis in 2003 and was appointed Chief Executive Officer in March 2013 at which time he was Chief Operating Officer
- Previously held country and regional management roles at Novartis Hungary, Asia Pacific and Australia



#### Jana Baskar - Chief Medical Officer

- 20+ years' experience both in clinical medicine and the biopharmaceutical industry
- Broad therapeutic knowledge and significant clinical research expertise having worked in several different specialties
- Former Medical Director at Novartis Oncology in Australia; former Medical Director for IQVIA in Australia and New Zealand



## Wolfgang Jarolimek - Drug Discovery

Read more on the

- 20+ years' experience in pharmaceutical drug discovery and published more than 30 peer reviewed articles
- Previously Director of Assay Development and Compound Profiling at the GlaxoSmithKline Centre of Excellence in Drug Discovery in Verona, Italy
- Spent 8 years as post-doc at the Max-Plank Institute in Munich, Germany; Baylor College of Medicine, Houston, Texas; Rammelkamp Centre, Cleveland Ohio; and University of Heidelberg, Germany



## David McGarvey – CFO

- more than 30 years' experience building Australian based companies from inception to globally successful enterprises
- joined Pharmaxis as Chief Financial Officer and Company Secretary in December 2002
- previously Chief Financial Officer of the Filtration and Separations
   Division of US Filter (1998-2002), and Memtec Limited (1985-1998)
- commenced career at PricewaterhouseCoopers



## Kristen Morgan – Alliance Management

- more than 20 years' experience in the pharmaceutical industry having previously held a senior role in medical affairs at Sanofi-Aventis, and a commercial sales role at GlaxoSmithKline
- responsibility for alliance management and medical and regulatory affairs



## **Dieter Hamprecht – Head of Chemistry**

- 20+ years' experience with small molecule and peptide drug discovery, contributed to greater than 10 drug candidates brought to development and co-inventor of 50 patent families, co-author of 30+ scientific publications
- Previously Managing Director Boehringer Ingelheim's research group in Milan
- Senior medicinal chemistry positions at GSK

# **Financials**

## Income statement highlights

Pariods anded (A\$'000) unaudited	Twelve	Twelve months		
Periods ended (A\$'000) - unaudited	Jun-22	Jun-21		
Segment Financials				
New drug development				
Oral LOX (external costs)	(5,431)	(2,521)		
Other program external costs (net of grants)	(1,712)	(1,850)		
Employee costs	(2,943)	(3,270)		
Overhead	(374)	(396)		
R&D tax credit and other income	5,600	148		
EBITDA	(4,859)	(7,889)		
Mannitol respiratory business				
Sales	7,427	6,680		
Other revenue and income	2,342	15,986		
	9,769	22,666		
Expenses – employee costs	(4,760)	(5,558)		
Expenses – manufacturing purchases	(2,729)	(1,168)		
Expenses – other	(3,584)	(4,483)		
EBITDA	(1,304)	11,457		
Corporate – EBITDA	(4,080)	(3,793)		
Total Adjusted EBITDA	(10,243)	(225)		
Net profit (loss)	(1,934)	(2,970)		

## Financials

## Cash

Periods ended (A\$'000)	Twelve months		
Perious ended (A\$ 000)	Jun-22	Jun-21	
Cash			
Cash at period end	8,937	18,712	
Cash received/receivable post period end			
2022 R&D tax credit - expected H2 CF 2022	4,900		
Exercise of Orbital option by Aptar - August 2022	7,031		
Proforma cash at period end	20,868		
Cash Flow Statement Highlights			
Operations			
Receipts from customers	8,313	7,242	
R&D tax incentive		5,048	
Milestone payments	340	13,844	
Sale of distribution rights	2,562	1,365	
Other	1,005	236	
Payments to suppliers, employees etc (net)	(28,322)	(24,663)	
Total operations	(16,102)	3,072	
Investing (capex & patents)	(306)	(644)	
Finance lease payments <sup>1</sup>	(2,379)	(2,305)	
Financing agreement payments <sup>2</sup>	(62)	(240)	
Share issue - net	9,074	4,065	
Net increase (decrease) in cash	(9,775)	3,948	

- 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 to March 2028

## Risks

Pharmaxis is developing drugs targeting inflammation, fibrosis and cancer indications and whilst some of these activities have passed pre-clinical testing and phase 1 clinical studies they have not yet demonstrated clinical proof of concept in patients. Pharmaxis' business is subject to a number of significant risk factors both specific to its business and of a general nature.

As such, potential investors should be aware that subscribing for securities in the Company involves a number of risks. Prior to deciding whether to apply for securities, potential investors should read this presentation in its entirety and review all announcements made to the ASX by the Company in order to gain an understanding of the Company, its activities, operations, financial position and prospects.

Below are described some of the potential risks associated with investing in the Company. The Company is subject to risks that are specific to its business. There are also risks that are associated with external events unrelated to the usual course of the Company's business or that are common to all investments in equity securities and not specific to an investment in the Company.

If any of these risks were to occur, the future operating and financial performance and prospects of the Company as well as the value of its securities could be materially and adversely affected and you could lose part or all of your investment in the Company. Given the current stage of development of the Company, investors should be aware that an investment in Pharmaxis is highly speculative. Whilst some of the risk factors may be mitigated by appropriate commercial action, many are either wholly or in part outside of the control of the Company and the Directors.

Investors should consider consulting their professional advisers before deciding whether to apply for securities.

No guarantee as to maintenance of or appreciation in value, the payment of dividends or return of capital of the Company's securities is provided. Further, there can be no guarantee that the Company will achieve its stated objectives or that any forward-looking statement will eventuate.

#### (a) Overview

Pharmaxis' business success is currently substantially dependent on its ability to successfully advance the clinical development of PXS-5505, PXS-6302 and PXS-4728 in a timely manner. Five clinical trials with respect to these product candidates have or will soon commence. There is a risk that the clinical development of all or some of these product candidates or any of our other product candidates that it may develop in the future, may not be successful, may be delayed or may cost more than anticipated.

Pharmaxis' strategy involves advancing a pipeline of development assets, including PXS-5505, PXS-6302 and PXS-4728, through clinical development to the point where it is able to enter into collaborative partnerships deals and strategic alliances with other lifescience companies to advance the programs and enable us to maintain our financial and operational capacity. There is a risk that Pharmaxis may not be able to enter into these sorts of collaborative partnership deals, on acceptable terms, or at all.

There is a risk that the product candidates may not receive the regulatory approvals required to commercialise them, or that such regulatory approval may be delayed. Even if regulatory approval is obtained, there is a risk that the products are not a commercial success.

Pharmaxis' business is currently substantially dependent on the successful commercialisation of Aridol and Bronchitol to generate sales revenue that offsets its expenses of conducting that business unit (mannitol segment). Pharmaxis' revenues from that business unit haves not grown as initially expected and there is a risk that the business unit will continue not to be profitable.

#### (b) The clinical development of Pharmaxis' product candidates may not be successful

Before obtaining regulatory approval for the commercial sale of any of the product candidates Pharmaxis is developing, it is necessary to complete preclinical development and extensive clinical trials in humans to demonstrate the safety and efficacy of the relevant product. Clinical trials are subject to extensive regulation, are expensive, time consuming, subject to delay and their outcome uncertain. Failure can occur at any stage of the clinical testing or approval process. Phase I clinical trials are not primarily designed to test the efficacy of a product candidate but rather to test safety, to study pharmacokinetics and pharmacodynamics and to understand the product candidate's side effects at various doses and schedules. Negative or inconclusive results or adverse medical events during a clinical trial could cause the clinical trial to be delayed, redone or terminated. Success in pre-clinical and early clinical trials is not a guarantee of future results nor does it ensure that later large scale trials will be successful.

The Company is currently involved in 5 clinical trials which are either recruiting or that it expects to commence later in 2022 or in 2023. These trials comprise a phase II trial of PXS-5505 in myelofibrosis, an investigator initiated phase 1b/2 trial of PXS-5505 in liver cancer, two phase Ic trials of PXS-6302 in scarring and a phase II trial of PXS-4728 in a severe sleep disorder that potentially leads to neurodegenerative diseases. These clinical trials (and future clinical trials) may not show sufficient safety or efficacy to:

- warrant progressing to the next phase of development;
- enable the Company to secure a collaborative partnership deal with a lifesciences company to enable the continued clinical development of any given product candidate to continue; or
- obtain regulatory approval to sell the product.

This may mean that Pharmaxis is unable to continue the development of one or more of its product candidates or generate revenue from those product candidates.



#### (c) The time and cost to undertake clinical trials and obtain regulatory approval may be significantly more than expected

The length of time and the cost necessary to complete clinical trials and to submit an application for marketing approval may vary significantly based on the type, complexity and novelty of the product candidate involved, as well as other factors. Due to the Company's reliance on contract research organisations, hospitals and investigators to conduct clinical trials, Pharmaxis is unable to directly control the timing, conduct and expense of its clinical trials. There are numerous factors that could affect the timing of the commencement, performance and completion of clinical trials which may delay the clinical trials or prevent Pharmaxis from completing these trials successfully, which include:

- any inability to secure a collaborative partnership deal at the appropriate time to enable the clinical development of any given product candidate to continue;
- delays in securing clinical investigators or trial sites for the Company's clinical trials, delays in obtaining approvals for trials;
- slower than anticipated recruitment of patients who meet the trial eligibility criteria or the loss of patients during the course of the clinical trials;
- the requirement to repeat clinical trials or undertake additional large clinical trials;
- unforeseen safety issues or adverse side effects or fatalities;
- shortages of available product supply of the necessary standard; and
- problems with investigator or patient compliance with the trial protocols.

#### (d) Pharmaxis may be unable to enter into collaborative partnership deals

An important element of Pharmaxis' strategy involves advancing a pipeline of product candidates through clinical development to the point where it is able to enter into collaborative partnerships deals and strategic alliances with other lifescience companies that can advance our programs and enable us to maintain our financial and operational capacity. These collaboration partners may be asked to assist with or take full responsibility for the clinical development, regulatory approval and commercialisation of a product or alternatively to assist with funding or performing clinical trials, manufacturing, regulatory approvals or product marketing. Generally, Pharmaxis will seek to enter into such partnership arrangements before entering into a phase III trial, but it may seek to do so earlier or later depending on the circumstances. Pharmaxis may not be able to negotiate these sorts of deals on acceptable terms, if at all, and cannot guarantee that any such partners will perform as required and meet commercialisation goals.

Even if Pharmaxis is successful in entering into such deals, these arrangements may result in Pharmaxis receiving less revenue than if it sold such products directly, may place the development and commercialisation of its products outside its control, may require it to relinquish important rights or may otherwise be on terms unfavourable to it.

The Company has demonstrated the value of the strategy when Boehringer Ingelheim acquired the development asset BI 1467335 from Pharmaxis in 2015. However, even after such success in which the Company received a total of A\$83 million, ongoing risks remain. In that case, in 2019 Boehringer Ingelheim determined to cease development of BI 1467335 and returned the asset to Pharmaxis. As a result, the Company is no longer receiving payments in connection with that transaction and the development prospects of that asset in NASH have ceased.

#### (e) Pharmaxis may not be successful in developing or securing new product candidates

Although the Company already has an extensive product candidate pipeline, its continues to spend limited resources developing new product candidates. From time to time it also considers in-licensing potential new product candidates. There is a risk that its research and development programs may not yield, or that it may not be able to in-license, additional product candidates suitable for further investigation through clinical trials.

### (f) Early stage company with limited revenue

Even though Pharmaxis has been in existence for some time, it remains at an early stage of its development as a clinical stage drug development company. The Company's current sole source of income from the sale of products is from Aridol and Bronchitol (the mannitol business unit). The sales of these products are insufficient to sustain the business efforts of the Company and to date, the mannitol business unit has operated at a loss.

Pharmaxis' ability to generate sufficient revenue in the future depends on a number of factors, including:

- the successful clinical development of its product candidates;
- its ability to secure collaborative partnership deals;
- the ability of Pharmaxis or its partners to obtain all necessary regulatory marketing authorisations for the products in a timely manner as well as other approvals concerning pricing and reimbursement;
- the ability to manufacture sufficient quantities of products to the required standard and at acceptable cost levels;
- the success of products developed by Pharmaxis and its partners in the market; and
- ongoing success in researching and developing new product candidates.

There is a risk that Pharmaxis will continue to incur losses from its operations and may not achieve or maintain profitability. Pharmaxis expects its expenses to increase in the short term in connection with continuing conduct of research and development projects and clinical trials. Over the longer term, Pharmaxis' costs will fluctuate, primarily dependent on the number, type and size of clinical trials, preclinical development and research projects being undertaken.

#### (g) Capital requirements

The funds raised under this offer is intended to fund the Company's current clinical study in myelofibrosis as well as other clinical studies in scarring, liver cancer and a severe sleep disorder that potentially leads to neurodegenerative diseases (eg Parkinson's disease), and general working capital purposes.

To achieve its goals, Pharmaxis will in the future require substantial additional funds which may be dilutive or that may not be available to Pharmaxis on favourable terms or at all. Its future funding requirements will depend on many factors and the timing of any such funding will depend on the success of its clinical programs and whether it is able to enter into collaborative partnership agreements. If Pharmaxis is unable to obtain additional funds when required, Pharmaxis may be forced to delay, reduce the scope or eliminate one or more clinical trials or research and development programs or future commercialisation efforts.

The phase II trial of PXS-4728 in severe sleep disorders that leads to neurodegenerative diseases is being mainly funded by Parkinson's UK. The funding is provided at various milestones. If this funding agreement was terminated, including for Pharmaxis' unremedied breach of the agreement, Pharmaxis would be forced to delay, reduce the scope or eliminate the trial.



#### (h) Dependence on distributors for sales of Aridol and Bronchitol

Pharmaxis currently relies on distributors to perform sales, marketing, distribution and supply activities for Aridol and Bronchitol. As a result, Pharmaxis has a lower degree of control over these activities than if it was conducting them directly. If these third parties are not successful in their commercialisation activities, do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, or if the third parties need to be replaced, Pharmaxis' commercialisation efforts for Aridol and Bronchitol may be severely compromised. There is no guarantee that Pharmaxis would be able to enter into alternative arrangements if required, on acceptable terms, or at all.

The US market is the largest market for Bronchitol. Bronchitol was approved by the US FDA in October 2020 however the full scale launch of the product was delayed as a result of the COVID-19 pandemic which restricted the ability of potential Bronchitol patients to routinely access medical facilities. Although the product is now launched in the US, sales growth continues to be hampered by the effects of the COVID-19 pandemic. Russia is also an important market for Bronchitol. Although sales of Bronchitol have continued since Russia's invasion of Ukraine, any escalation or changes in that conflict, additional sanctions or changes in policy, may impact our continued ability to commercialise Bronchitol in Russia which would significantly reduce our Bronchitol revenues.

## (i) Regulatory approvals

The process to obtain regulatory authorisation is expensive, complex, lengthy and the outcomes uncertain. Failure can occur at any stage of the clinical testing or approval process. Pharmaxis and its partners (if any) may not be able to obtain marketing authorisations for some or all of its product candidates in key jurisdictions, or those authorisations may be delayed or subject to significant limitations in the form of narrow indications, warnings, precautions or contra-indications with respect to conditions of use.

## (j) Ongoing regulatory issues

Even after products receive regulatory authorisation, Pharmaxis and its collaborative partners may still face developmental and ongoing regulatory compliance difficulties. Regulatory agencies subject a marketed product, its manufacturer and the manufacturer's facilities to continual review and periodic inspections. Potentially costly follow-ups or post-marketing clinical studies may be required and previously unknown problems may result in restrictions on the marketing of the product and could include product withdrawal.

If Pharmaxis fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend Pharmaxis' regulatory authorisation or restrict or change the approved indications for use or impose additional safety reporting requirements;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed;
- impose restrictions on Pharmaxis' or its partner's operations, including closing Pharmaxis' or its contract manufacturers' facilities or terminating its licenses to manufacture Good Manufacturing Practice grade material; or
- seize or detain products or require a product recall.

In addition, the law or regulatory policies governing pharmaceuticals may change. New regulatory requirements or additional regulations may be enacted that could prevent or delay regulatory approval of Pharmaxis' products or that may otherwise impact on Pharmaxis' ability to market, distribute and sell product. Pharmaxis cannot predict the likelihood, nature or extent of adverse government regulation that may arise.

#### (k) Even if a product is approved, the product may not warrant launch or even if launched, may not be successful in the market

There is a risk that the product candidates Pharmaxis is developing and future product candidates, even if they receive regulatory approval may not gain adequate market acceptance. The degree of market acceptance will depend on a variety of factors, including: the ability to demonstrate safety and efficacy and the prevalence and severity of any side effects; the level of support from clinicians; the relative convenience and ease of administration; cost-effectiveness compared to other treatments; the availability of reimbursement from national health authorities; the timing of market introduction and clinical profile of competitive products; and the success of marketing and sales efforts. Additionally, it is difficult to determine the portion of the patient population that might use Pharmaxis' products and there is a risk that Pharmaxis' estimates do not accurately reflect the number of patients in the target markets.

#### (I) Pricing and reimbursement

The commercial success of any products obtain regulatory approval, is substantially dependent on achieving acceptable pricing and whether acceptable third-party coverage and reimbursement is available from government bodies, private health insurers and other third-parties. This process of obtaining pricing for products is time consuming and the outcomes in certain jurisdictions may not be sufficient to warrant the marketing of products in that jurisdiction.

An inability to obtain or delays in obtaining satisfactory pricing and reimbursement in certain jurisdictions may impair Pharmaxis and any partner's ability to effectively commercialize products in those jurisdictions. Even if products receive acceptable pricing and reimbursement, pricing and reimbursement levels are subject to change.

## (m)Manufacturing

Pharmaxis, its partners' or their contract manufacturers and suppliers, may fail to achieve and maintain required production yields or manufacturing standards for a number of reasons, which could result in patient injury or death, product recalls or withdrawals, product shortages, delays or failures in product testing or delivery or other problems that could seriously harm Pharmaxis' (and its partners') business. Any interruption to Pharmaxis' or its collaboration partner's manufacturing capability could result in the cancellation of shipments and loss of product, resulting in delays and additional costs.

#### (n) Competition

Pharmaxis conducts business in a highly competitive industry in which there are a number of well established competitors that have significantly greater financial resources, sales and marketing organisations, market penetration and development capabilities, as well as broader product offerings and greater market and brand presence. There can be no assurances given in respect of Pharmaxis' ability to compete.

#### (o) Product liability claims and insurance

Pharmaxis and its collaboration partners faces product liability exposure with respect to its products and product candidates. Regardless of merit or eventual outcome, liability claims may result in decreased demand for Pharmaxis and its partners' products; injury to Pharmaxis' and its partners' reputation; withdrawal of clinical trial participants; costly litigation and potential contractual disputes; substantial monetary awards to patients and others; loss of revenues; and an inability to commercialise. Pharmaxis and its partners' may not be able to maintain insurance coverage at a reasonable cost nor obtain suitable or reasonable insurance coverage in respect of any liability that may arise and any claim for damages could be substantial.



#### (p) Patents and trade secrets

Pharmaxis uses patents or trade secrets to protect its technologies from unauthorised use by third parties. The term of patents may expire or may be challenged, invalidated or circumvented. There can be no assurances that Pharmaxis' patents will afford it significant commercial protection for its products.

#### (q) Enforcement and infringement of intellectual property

Third parties may own or control patents or patent applications that Pharmaxis or its partners may be required to license to commercialise product candidates, that Pharmaxis or its partners may infringe, or that could result in litigation that would be costly and time consuming.

As a result of intellectual property infringement claims, or to avoid potential claims, Pharmaxis or its collaboration partners might be prohibited from selling or licensing a product; required to expend considerable amounts of money in defending claims; required to pay substantial royalties or license fees; required to pay substantial monetary damages; or required to redesign the product so it does not infringe, which may not be possible or could require substantial funds and time.

## (r) Dependence upon key personnel

The key personnel, particularly in the Company's research and development and clinical areas, have a high degree of expertise and the Company is reliant on their continued service to maintain and develop its business. The loss of a key employee or the inability to recruit and retain high caliber staff to manage future anticipated growth could have a material adverse effect on the Company.

The additions of new employees and departures of existing employees, particularly in key positions, can be disruptive and could also have a material adverse effect on the Company. Increases in recruitment, wages and contractor costs may adversely impact upon the financial performance of the Company.

## (s) Litigation

There has been substantial litigation and other proceedings in the pharmaceutical and biotechnology industries. Defending against litigation and other third party claims would be costly and time consuming and would divert management's attention from our business, which could lead to delays in our development or commercialisation efforts. If third parties are successful in their claims, Pharmaxis might have to pay substantial damages or take other actions that are adverse to the Pharmaxis business.

## (t) Change in laws

Pharmaxis' business and the business or the third parties with which it operates are subject to the laws and regulations in a number of jurisdictions. Unforeseen changes in laws and government policy both in Australia, the EU, the US and elsewhere, including material and unforeseen changes to licensing and approval requirements or regulations relating to clinical trials, manufacturing, product approval and pricing could materially impact Pharmaxis' operations, assets, contracts and profitability.



# Foreign Jurisdiction Selling Restrictions

#### **International Offer Restrictions**

This document does not constitute an offer of new ordinary shares ("New Shares") of the Company in any jurisdiction in which it would be unlawful. In particular, this document may not be distributed to any person, and the New Shares may not be offered or sold, in any country outside Australia except to the extent permitted below.

#### Cayman Islands

No offer or invitation to subscribe for New Shares may be made to the public in the Cayman Islands or in any manner that would constitute carrying on business in the Cayman Islands.

#### **Hong Kong**

WARNING: This document has not been, and will not be, registered as a prospectus under the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong, nor has it been authorised by the Securities and Futures Commission in Hong Kong pursuant to the Securities and Futures Ordinance (Cap. 571) of the Laws of Hong Kong (the "SFO"). Accordingly, this document may not be distributed, and the New Shares may not be offered or sold, in Hong Kong other than to "professional investors" (as defined in the SFO and any rules made under that ordinance).

No advertisement, invitation or document relating to the New Shares has been or will be issued, or has been or will be in the possession of any person for the purpose of issue, in Hong Kong or elsewhere that is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to New Shares that are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors. No person allotted New Shares may sell, or offer to sell, such securities in circumstances that amount to an offer to the public in Hong Kong within six months following the date of issue of such securities.

The contents of this document have not been reviewed by any Hong Kong regulatory authority. You are advised to exercise caution in relation to the offer. If you are in doubt about any contents of this document, you should obtain independent professional advice.

## **New Zealand**

This document has not been registered, filed with or approved by any New Zealand regulatory authority under the Financial Markets Conduct Act 2013 (the "FMC Act").

The New Shares are not being offered or sold in New Zealand (or allotted with a view to being offered for sale in New Zealand) other than to a person who:

- is an investment business within the meaning of clause 37 of Schedule 1 of the FMC Act;
- meets the investment activity criteria specified in clause 38 of Schedule 1 of the FMC Act;
- is large within the meaning of clause 39 of Schedule 1 of the FMC Act;
- is a government agency within the meaning of clause 40 of Schedule 1 of the FMC Act; or
- is an eligible investor within the meaning of clause 41 of Schedule 1 of the FMC Act.



# Foreign Jurisdiction Selling Restrictions

#### **United Kingdom**

not apply to the Company.

Neither this document nor any other document relating to the offer has been delivered for approval to the Financial Conduct Authority in the United Kingdom and no prospectus (within the meaning of section 85 of the Financial Services and Markets Act 2000, as amended ("FSMA")) has been published or is intended to be published in respect of the New Shares.

The New Shares may not be offered or sold in the United Kingdom by means of this document or any other document, except in circumstances that do not require the publication of a prospectus under section 86(1) of the FSMA. This document is issued on a confidential basis in the United Kingdom to "qualified investors" within the meaning of Article 2(e) of the UK Prospectus Regulation. This document may not be distributed or reproduced, in whole or in part, nor may its contents be disclosed by recipients, to any other person in the United Kingdom. Any invitation or inducement to engage in investment activity (within the meaning of section 21 of the FSMA) received in connection with the issue or sale of the New Shares has only been communicated or caused to be communicated and will only be communicated or caused to be communicated in the United Kingdom in circumstances in which section 21(1) of the FSMA does

In the United Kingdom, this document is being distributed only to, and is directed at, persons (i) who have professional experience in matters relating to investments falling within Article 19(5) (investment professionals) of the Financial Services and Markets Act 2000 (Financial Promotions) Order 2005 ("FPO"), (ii) who fall within the categories of persons referred to in Article 49(2)(a) to (d) (high net worth companies, unincorporated associations, etc.) of the FPO or (iii) to whom it may otherwise be lawfully communicated (together "relevant persons"). The investment to which this document relates is available only to relevant persons who is not a relevant person should not act or rely on this document.

#### **United States**

This document does not constitute an offer to sell, or a solicitation of an offer to buy, securities in the United States. The New Shares have not been, and will not be, registered under the US Securities Act of 1933 or the securities laws of any state or other jurisdiction of the United States. Accordingly, the New Shares may not be offered or sold in the United States except in transactions exempt from, or not subject to, the registration requirements of the US Securities Act and applicable US state securities laws.

The New Shares will only be offered and sold in the United States to:

- "institutional accredited investors" within the meaning of Rule 501(a)(1), (2), (3), (7), (8), (9) and (12) under the US Securities Act; and
- dealers or other professional fiduciaries organized or incorporated in the United States that are acting for a discretionary or similar account (other than an estate or trust) held for the benefit or account of persons that are not US persons and for which they exercise investment discretion, within the meaning of Rule 902(k)(2)(i) of Regulation S under the US Securities Act.





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