



## Investor Presentation

**pharmaxis**

developing breakthrough treatments for fibrosis and inflammation

Investor Presentation | 22 March 2022

Gary Phillips CEO

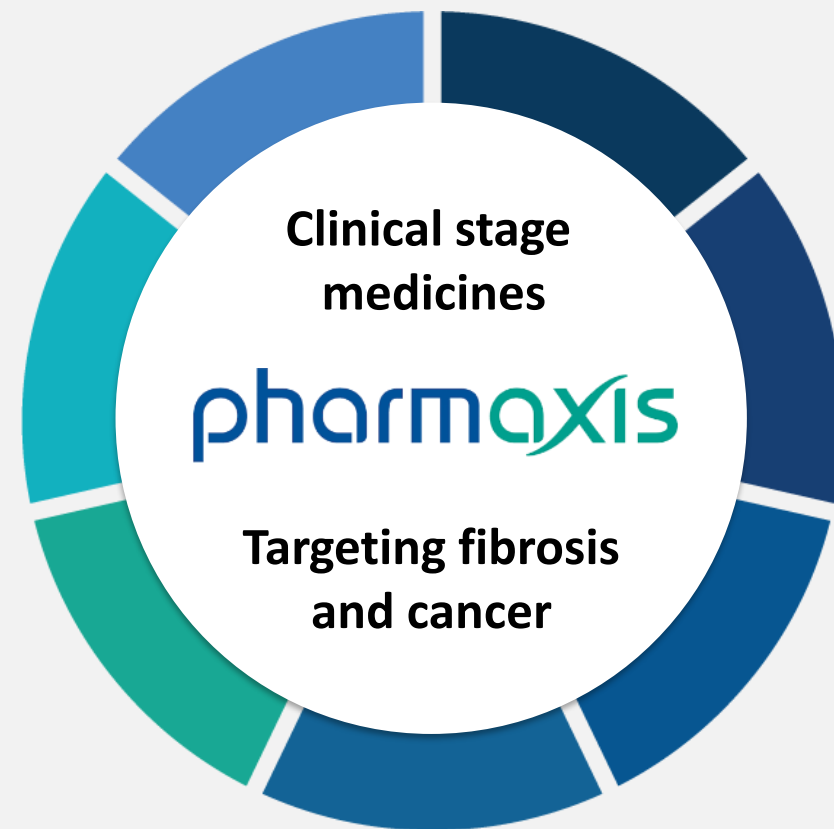
## Forward looking statement

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.

## Executive Summary

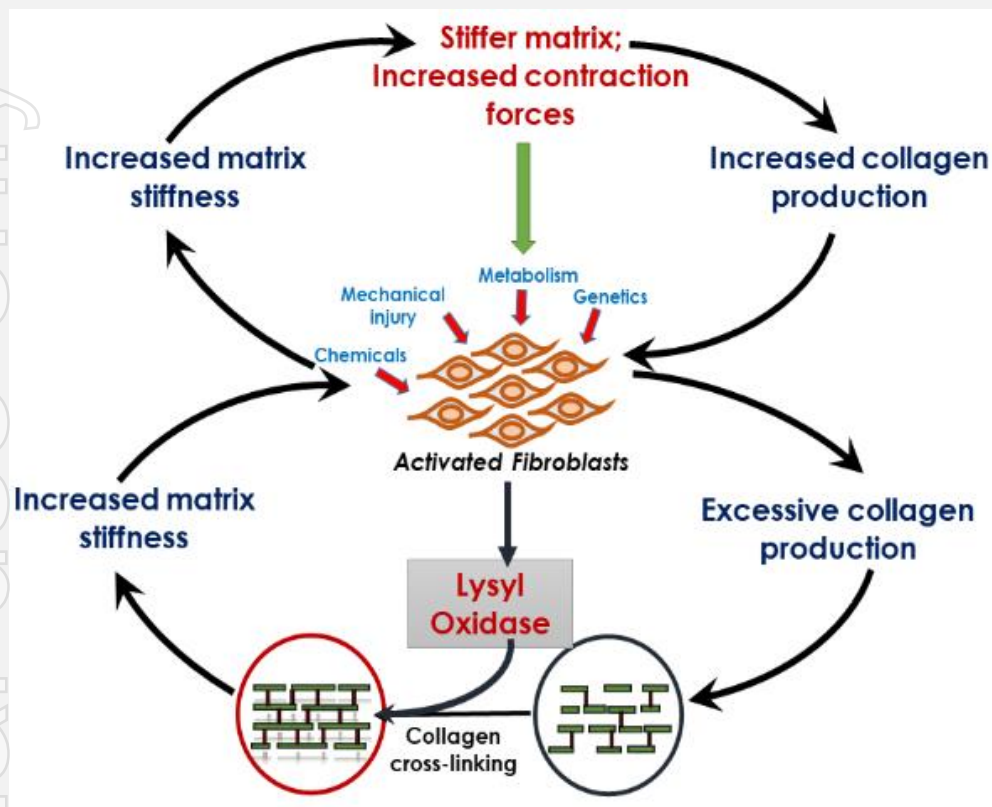
- Pharmaxis is a clinical stage drug development company targeting fibrosis and cancer indications with first in class or best in class small molecule drugs in markets of high value
- Pharmaxis is the global leader in fibrosis driven by lysyl oxidase enzymes having invested in a multi year research program leveraged with extensive external scientific collaborations
- Pharmaxis has 4 studies planned for 2022 that will lead to near term value opportunities
  - Lead asset PXS-5505 is in a multinational phase 2 trial – a breakthrough clinical program with disease modifying potential in Myelofibrosis
  - IND approval to commence US investigator led phase 2 trial in liver cancer with PXS-5505 as first line treatment added to existing chemotherapy.
  - Topical drug PXS-6302 is in a phase 1c trial in patients with potential to improve function and appearance of established scars with a study in burns patients to follow later this year.
- Specific corporate strategy to deliver non-dilutive cash and cost savings from commercial stage mannitol business
- Pharmaxis is well positioned to fund its focused clinical program



# 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 is preventable through lysyl oxidase inhibition and at the heart of a true anti-fibrotic therapy

### ■ PXS-5505

- Oral dosage form – one capsule twice a day
- Patent 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 – one application per day
- Patent 2019
- Strong pre clinical evidence in models of skin fibrosis and scarring
- Potential in prevention of scar formation and modification of existing scars
- Phase 1 data demonstrates a safe, well tolerated drug that gives full inhibition of LOX enzymes in the skin with minimal systemic exposure

# Myelofibrosis background

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

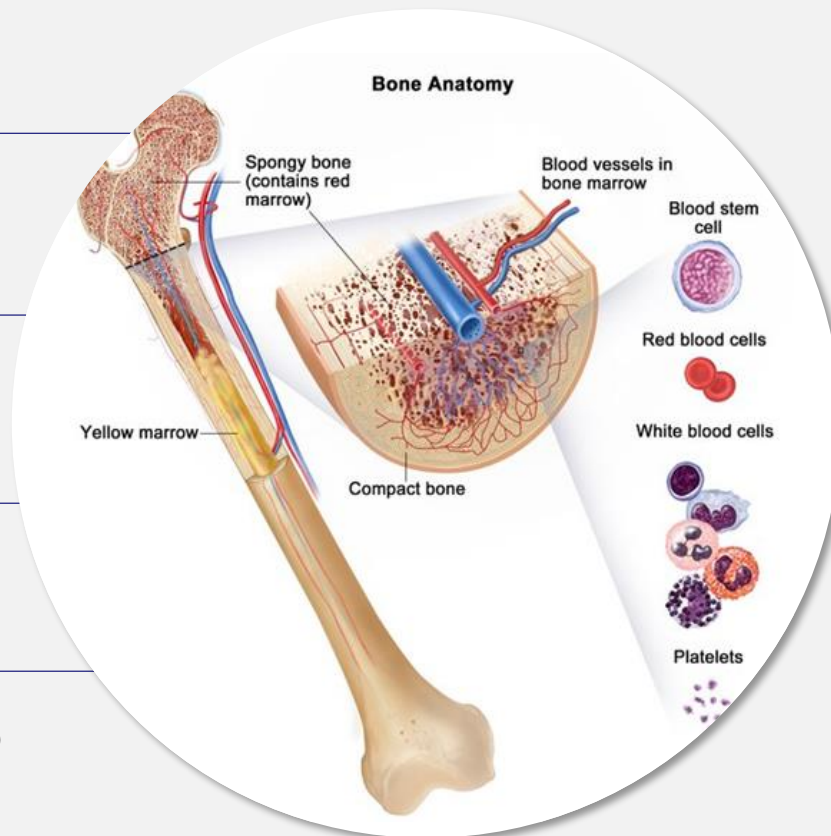
## KEY FACTS

- Affects 15 in 1m people worldwide

- 5 Years Median survival

- Age of onset 50 – 80

- 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

## 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

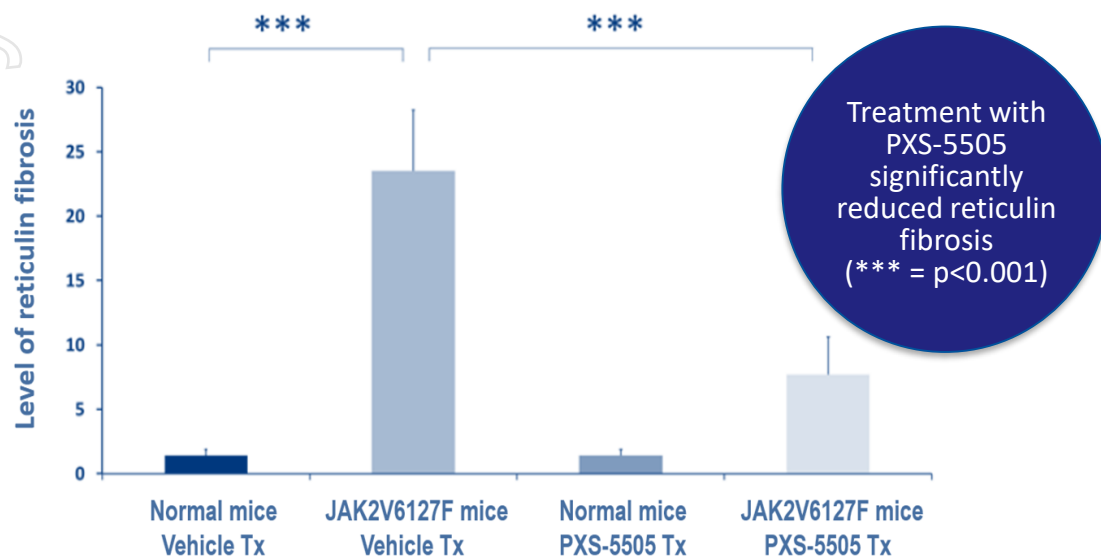
## Commercial Opportunity

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

# 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

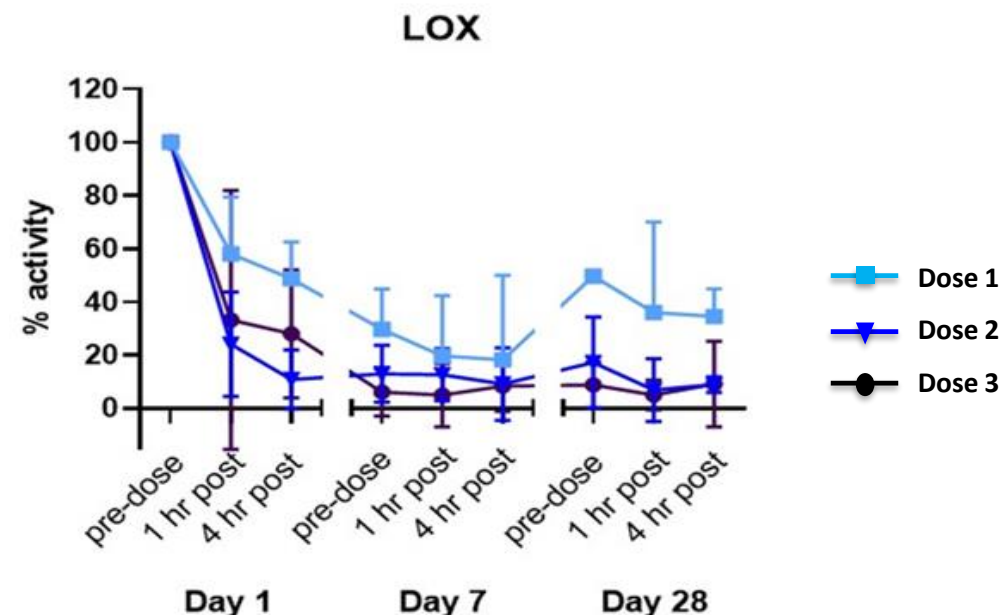


*"None of the drugs approved to date consistently or meaningfully alter the fibrosis that defines this disease. PXS-5505 has a novel mechanism of action by fully inhibiting all LOX enzymes.*

*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 expansion 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

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

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

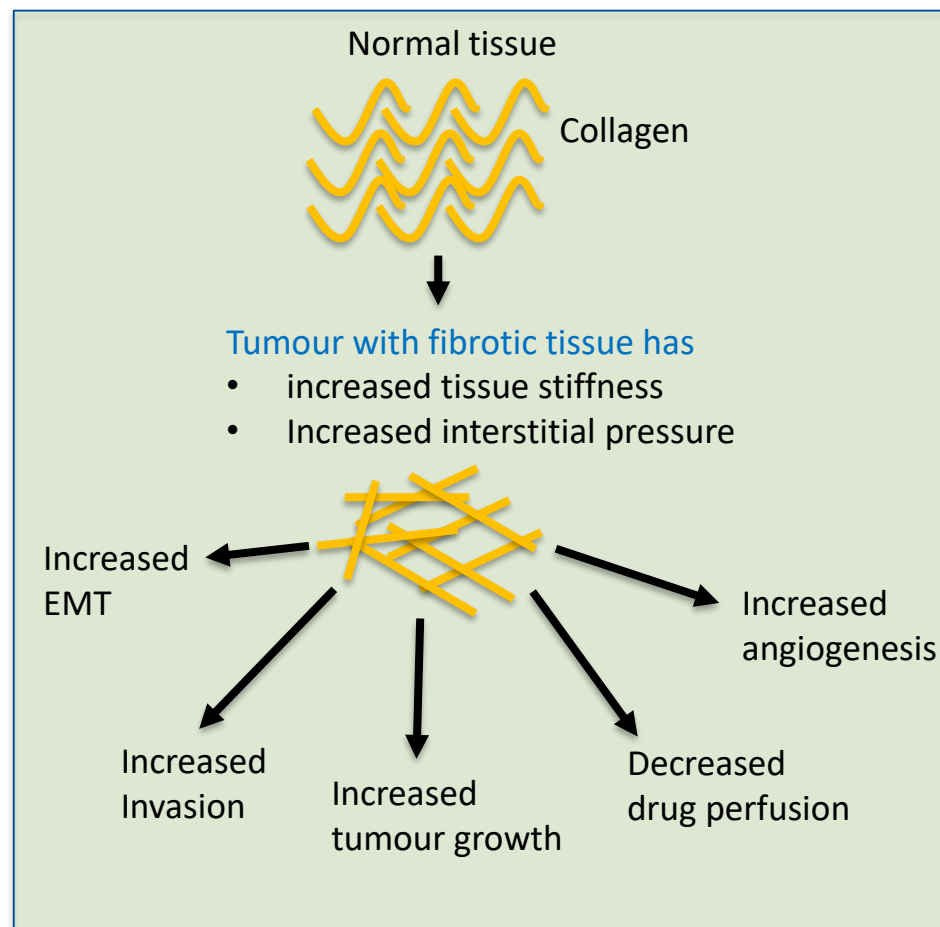
<sup>2</sup> Unsuitable = ineligible for JAKi treatment, intolerant of JAKi treatment, relapsed during JAKi treatment, or refractory to JAKi treatment. JAKi – Janus Kinase inhibitor, MF myelofibrosis, ET Essential Thrombocythaemia, PV polycythaemia vera



# 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.
- 4th leading cause of cancer-related mortality worldwide with a 19.6% 5-year relative survival
- HCC is a stromal (fibrotic) tumour
  - 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 pre-clinical model significantly **improves survival, delays tumor 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

# 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



“We now understand from our research that even scars which are stable and many years old are in fact replenishing a significant proportion of mature, stiff collagen in a matter of a few months.”

- 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 (data on file)

- 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



# Four 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             | Year end 2022 |
|          | 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 Q2 2022  | 2H 2023       |
| 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             | Q4 2022       |
|          | 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 mid 2022 | 1H 2023       |

# Shareholders & cash



| Financial Information  | 18 Mar 22   |
|--|-------------|
| ASX Code   | PXS         |
| Share price  | \$0.085     |
| Liquidity (turnover last 12 months)  | 198m shares |
| Market Cap   | A\$47m      |
| Cash balance (31 Dec 2021)   | A\$21m      |
| Enterprise value   | A\$26m      |
| Clinical development program supported by:   |             |
| <ul style="list-style-type: none"><li>• Mannitol business* forecast to provide ongoing positive EBITDA growing to \$10m in 5 - 6 years</li><li>• R&amp;D tax credits</li><li>• Strategy of partnering deals with pipeline assets</li></ul> |             |

| Institutional Ownership              | 18 Mar 22  |
|--------------------------------------|------------|
| BVF Partners LP                      | 18%        |
| Karst Peak Capital Limited           | 12%        |
| D&A Income Limited                   | 8%         |
| <b>Total Institutional Ownership</b> | <b>41%</b> |






## Share Price

Chart generated on 29/1/2022 at 10:33 am



# Myelofibrosis – examples of other programs

PXS-5505 unique mechanism of action designed for disease modification and good tolerability

| Company   | Market cap <sup>(1)</sup>                 | Bourse         | Asset      | Description          | Current clinical phase |
|---|---|----------------|------------|----------------------|------------------------|
|  KEROS THERAPEUTICS            | \$1.3bn                                   | Nasdaq         | KER-050    | TGF-β ligand trap    | Phase 2                |
|  Constellation PHARMACEUTICALS | Acquired by MorphoSys for \$1.7b in Q3 21 | Nasdaq         | CPI-0610   | BET inhibitor        | Phase 3                |
|  KARTOS THERAPEUTICS           | \$0.7bn <sup>(2)</sup>                    | n.a. – private | KRT-232    | MDM2 antagonist      | Phase 3                |
|  geron                         | \$0.4bn                                   | Nasdaq         | Imetelstat | Telomerase inhibitor | Phase 3                |
|  pharmaxis                     | \$35m (A\$47m)                            | ASX            | PXS-5505   | LOX inhibitor        | Phase 2 commenced      |

PXS-5505 unique mechanism of action expected to deliver additional efficacy on top of existing standard of care (JAK 1/2 inhibitors) and/or known pipeline drugs without adding to tolerability issues

# Anticipated news flow: 2022

Multiple anticipated value inflection points

## PXS-5505 – anti cancer drug

- PXS-5505 phase 1c liver cancer (HCC) study – starts recruitment
- PXS-5505 phase 2a myelofibrosis study – fully recruited
- PXS-5505 phase 2a myelofibrosis study safety and efficacy data
- PXS-5505 publications by KOL's in other cancers
- Results of Charlie Teo Foundation funded research into PXS-5505 in glioblastoma

## PXS-6302 – scar treatment

- LOX topical drug PXS-6302 commences independent investigator patient studies - burns scars
- LOX topical drug PXS-6302 patient studies fully recruited – established and burns scars
- PXS-6302 publications by KOL's in scarring

## Other

- Mannitol business – appointment of new distributors
- Decision by Aptar whether to exercise (by Aug 22) option to license high payload inhaler for US\$2.5m plus royalties



developing breakthrough treatments for fibrosis and inflammation

Pharmaxis Ltd ABN 75 082 811 630

[www.pharmaxis.com.au](http://www.pharmaxis.com.au)



## Contacts

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David McGarvey

Chief Financial Officer

[david.mcgarvey@pharmaxis.com.au](mailto:david.mcgarvey@pharmaxis.com.au)



## Additional Information

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# Mannitol respiratory business (Bronchitol® and Aridol®)

Transformational impact of FDA Bronchitol approval (Oct 2020) – business segment cash flow positive from FY 2021 onwards

## 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
- Continue to pursue simplification of business model to reduce costs

## Segment EBITDA

- 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
- Chiesi approval /launch milestone payments US\$10m received FY 2021
- US sales commenced in Q2 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
- Three sales milestones totaling US\$15m payable on achieving annual sales thresholds

# Experienced Scientific Leadership Team

Significant global experience in drug development, commercialisation and partnering

## In senior management



### Wolfgang Jarolimek – Drug Discovery

- 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-Planck Institute in Munich, Germany; Baylor College of Medicine, Houston, Texas; Rammelkamp Centre, Cleveland Ohio; and University of Heidelberg, Germany



### 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



### Brett Charlton - Medical

- 25+ years' experience in clinical trial design and management
- Author of more than 80 scientific papers
- Founding Medical Director of the National Health Sciences Centre
- Previously held various positions with the Australian National University, Stanford University, the Baxter Centre for Medical Research, Royal Melbourne Hospital, and the Walter and Eliza Hall Institute

## On the board



### 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



### 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



### 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



# 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



## Will Delaat – Non-Executive Director

- 35+ years' experience in the global pharmaceutical industry
- Former CEO of Merck Australia
- Former chair of Medicines Australia and Pharmaceuticals Industry Council
- Joined Pharmaxis Board in 2008



## 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
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- Former Chief Medical Officer at Trimeris Inc and Tibotec Pharmaceuticals

# Financials

## Income statement highlights

| Periods ended (A\$'000)                      | Three months |         | Six months |         |
|--|--------------|---------|------------|---------|
|  | Sep-21       | Sep-20  | Sep-21     | Sep-20  |
| <b>Segment Financials</b>                    |              |         |            |         |
| <b>New drug development</b>                  |              |         |            |         |
| Oral LOX (external costs)                    | (1,102)      | (546)   | (2,569)    | (1,323) |
| Other program external costs (net of grants) | (462)        | (478)   | (765)      | (775)   |
| Employee costs                               | (602)        | (875)   | (1,317)    | (1,799) |
| Overhead                                     | (77)         | (145)   | (179)      | (238)   |
| R&D tax credit                               | -            | -       | -          | 148     |
| EBITDA                                       | (2,243)      | (2,044) | (4,830)    | (3,987) |
| <b>Mannitol respiratory business</b>         |              |         |            |         |
| Sales  | 2,526        | 2,425   | 5,798      | 3,086   |
| Other revenue and income                     | -            | 9,956   | 2,342      | 10,098  |
|  | 2,526        | 12,381  | 8,140      | 13,184  |
| Expenses – employee costs                    | (1,243)      | (1,529) | (2,440)    | (2,914) |
| Expenses – manufacturing purchases           | (1,038)      | (1,101) | (2,243)    | (1,172) |
| Expenses – other                             | (762)        | (1,162) | (1,904)    | (2,374) |
| EBITDA                                       | (517)        | 8,589   | 1,553      | 6,724   |
| <b>Corporate – EBITDA</b>                    | (1,895)      | (1,164) | (2,573)    | (2,024) |
| <b>Total Adjusted EBITDA</b>                 | (4,655)      | 5,381   | (5,850)    | 713     |
|  |              |         |            |         |
| <b>Net profit (loss)</b>                     | (5,677)      | 5,027   | (8,856)    | 46      |



# Financials

## Cash

| Periods ended (A\$'000) | Three months |        | Six months |        |
|-------------------------|--------------|--------|------------|--------|
|                         | Sep-21       | Sep-20 | Sep-21     | Sep-20 |

### Cash

|                 |        |        |        |        |
|-----------------|--------|--------|--------|--------|
| Cash period end | 20,866 | 18,249 | 20,866 | 18,249 |
|-----------------|--------|--------|--------|--------|

### Cash Flow Statement Highlights

|  |         |         |          |          |
|--|---------|---------|----------|----------|
| Operations                                 |         |         |          |          |
| Receipts from customers                    | 3,757   | 1,668   | 4,913    | 3,602    |
| R&D tax incentive                          | -       | 5,061   |          | 5,099    |
| Chiesi milestone                           | -       | 9,949   | -        | (10,958) |
| Sale of distribution rights                | -       | -       | 2,342    | -        |
| Other                                      | 202     | 15      | 920      | 36       |
|  | (7,696) | (6,335) | (13,857) | (27,330) |
| Payments to suppliers, employees etc (net) |         |         |          |          |
| Total operations                           | (3,737) | 10,358  | (5,682)  | (29,551) |
| Investing (capex & patents)                | (31)    | (181)   | (71)     | (281)    |
| Finance lease payments <sup>1</sup>        | (592)   | (573)   | (1,185)  | (1,147)  |
| Financing agreement payments <sup>2</sup>  | (5)     | (67)    | (8)      | (135)    |
| Share issue - net                          | 9,100   | -       | 9,100    | -        |
| Net increase (decrease) in cash            | 4,735   | 9,537   | 2,154    | (31,114) |

1. Lease over 20 Rodborough Rd (to May 2024) – total liability at 30 June 2021: \$6.3 million
2. NovaQuest financing – not repayable other than as % of US & EU Bronchitol revenue – up to 7 years



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