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 partnering our LOXL2 program or any of the other 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 has a successful track record of research, development and commercialisation of human healthcare products for the treatment and management of fibrotic and inflammatory diseases.

- **Drug Discovery Engine**
  - Leverage small molecule expertise and in house chemistry platform
  - Efficiencies from global academic & CRO networks
  - Target high value diseases with validated targets

- **Clinical Trials**
  - Utilise global experience and extensive clinical networks to execute value adding Phase 1 and 2 clinical trials

- **Value Generation**
  - Extensive Big Pharma network
  - Seek to partner after phase 1 or 2 to realise value and mitigate program and corporate risk
Why Pharmaxis?

Key factors that increase our probability of success

- **Strong Balance Sheet**
  - Closing cash at 30th September 2018: $47m

- **Experienced Management Team with a proven track record**
  - Biotech and Big Pharma experience
  - Established networks with Big Pharma inflammation and fibrosis executives
  - One major phase 1 deal already achieved

- **A promising pipeline of early – mid stage assets**
  - Leverages amine oxidase chemistry platform
  - 6 lead candidate compounds generated in last 5 years
    → 3 already in clinical development
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Pharmaxis Science – A Board Perspective

Dr Kathleen Metters
Pharmaxis Non Executive Director
Drug discovery capability

Significant experience in drug development, commercialisation and partnering

Drug discovery leadership

Wolfgang Jarolimek – Head of Drug Discovery, Pharmaxis
- Previously Director of Assay Development and Compound Profiling at the GlaxoSmithKline Centre of Excellence in Drug Discovery in Verona, Italy; Max-Plank Institute in Munich, Germany; Baylor College of Medicine, Houston, Texas; Rammelkamp Centre, Cleveland Ohio; and University of Heidelberg, Germany

Dieter Hamprecht – Head of Chemistry, Pharmaxis
- Previously Managing Director – Boehringer Ingelheim’s research group in Milan; senior medicinal chemistry positions at GSK

Scientific Advisory Board

Prof Jacob George
Professor of Hepatic Medicine – Westmead Millennium Institute, University of Sydney; Head of Dept of Gastroenterology and Hepatology – Westmead Hospital

Prof Carol Pollock
Chair, NSW Cardiovascular Research Network; Chair, Research Advisory Committee of ANZ Society of Nephrology, Chair, Northern Sydney Local Health District Board

Prof Andrew Boyle
Professor of Cardiovascular Medicine, Director of Priority Clinical Centre for Cardiovascular Health, University of Newcastle and John Hunter Hospital

Prof Darren Kelly
Associate Dean (Innovation and Enterprise), The University of Melbourne; Director of Innovation and Enterprise, Centre for Eye Research Australia; Director of Biomedical Research, Department of Medicine, St Vincent’s Hospital Melbourne. Former CEO of Fibrotech Ltd, CEO of OccuRx.

Dr Kathleen Metters
Formerly Senior Vice President and Head of Worldwide Basic Research for Merck & Co. Non executive Director, Pharmaxis Ltd

Dr Alan Robertson
Medicinal chemist with extensive global drug development experience including GSK, Faulding and Amrad. Inventor of migraine drug Zomig. CEO of Pharmaxis 2000 to 2013
Boehringer Ingelheim

Thomas Jensen

Project Manager IPM Cardiometabolic/CNS, Boehringer Ingelheim GmbH

Dr Petra Moroni-Zentgraf

Medical Director, Boehringer Ingelheim Pty Ltd
Boehringer Ingelheim development program for BI 1467335
Pharmaxis Investor Research Briefing
20th November 2018
Boehringer Ingelheim (BI) in brief

- **Family-owned global corporation**
- Founded 1885 in Ingelheim, Germany
- Focus on Human pharmaceuticals, Animal health and biopharmaceutical contract manufacturing
- Around 50,000 employees worldwide
- Four R&D sites worldwide
- R&D expenditure of around EUR 3.1 billion
- Net sales of nearly EUR 18.1 billion
- 181 affiliated companies worldwide

Status: 31.12.2017
BI investing in the global innovation community

Expanding our global community of innovation partners

- Increasing our emphasis on external partnerships
- EUR 1.5 billion designated for collaborations with external innovators\(^1\)
- Investing in enduring partnerships that create a culture for shared commercial success
- Building long-lasting relationships with our partners based on our Company values: respect, empathy, trust, passion
- Committing to sustained investment to support the next generation of medical breakthroughs

\(^1\) Investment designated to the end of 2020
BI research and development innovation: Four focus areas

- Cardiometabolic diseases
- Central nervous system diseases
- Immunology and respiratory diseases
- Oncology research and cancer immunology
BI 1467335 (formerly PXS-4728A)
– one compound in two indication areas

- Oral irreversible inhibitor of amine oxidase, copper containing 3 (AOC3)*
- Anti-inflammatory mechanism
- Discovered and investigated in Australian Phase I trials by Pharmaxis
- Acquired by Boehringer Ingelheim (BI) in May 2015
- BI 1467335 positioned as a compound in two of BIs future strategic Key and Emerging disease areas
  – Non-alcoholic steatohepatitis (NASH)
  – Diabetic Retinopathy (DR)

*Also known as vascular adhesion protein-1 (VAP-1) or semicarbazide-sensitive amine oxidase (SSAO)
NASH Progression

- Normal Liver
- Non-alcoholic fatty liver (NAFLD)
- NASH
- Cirrhosis
- Hepatocellular Carcinoma

Factors:
- Comorbidities
- Genetic factors
- Microbiota
- Lifestyle
- Diet

Stages:
- F1/mild
- F2/moderate
- F3/severe
- F4/cirrhosis

5-50 Years

Sources: Younossi et al., Hepatology 2016.
Incidence of Non-alcoholic fatty liver disease (NAFLD) has increased dramatically in the past two decades, and is now the most common liver disease in all Western countries.

Estimated that 30% of the general population has excess fat in their liver (NAFLD) → 10 to 30% of patients with NAFLD will progress to NASH → Approximately 1.5 – 6.45% of the general population may develop NASH.

People who are lean or children are affected by NAFLD and can develop NASH.

NASH prevalence is expected to grow with the increasing rate of obesity and DM → NASH is predicted to become the leading indication for liver transplant in the next few years.

Sources: Estes et al., Hepatology 2018; Younossi et al., Hepatology 2016
Treatment of NASH

Currently there are no approved medications for NASH

Current management approaches include...

- Maintain a healthy weight
- Follow a balanced diet that is low in sugar and saturated fat
- Increase physical activity as tolerated
- Avoid alcohol
- Omega 3 FA’s, Vitamin E (off label/OTC), Pioglitazone (off label)

Development of NASH therapies is highly competitive with a number of companies investigating a wide variety of MoAs confirming that the pathogenesis is not well understood

MoA: Mode of Action

Sources: Chalasani et al., Gastroenterology 2012

Boehringer Ingelheim presentation @ Pharmaxis Investor Research Briefing 20th November 2018
Pathogenesis of Diabetic Retinopathy

**Systemic Onset**

Hyperglycaemia
Increase in blood glucose initiates vascular disruptions

Microvascular Disruptions
Characterized by abnormal flow, disruptions in permeability, occlusions

Hypoxic Conditions
Reduced perfusion reduces $O_2$ and triggers inflammatory cytokine response

**Ocular Manifestation**

Non-Proliferative Diabetic Retinopathy (NPDR)
The result of damage to the small blood vessels and neurons of the retina

Retinal haemorrhages

Proliferative Diabetic Retinopathy (PDR)
Overgrowth new capillaries in response to increased hypoxia

Neovascularisation
Before Angiogenesis
After Angiogenesis

Sources: Healthline; Blausen; Samarasinghe, B., 2013; Plascyk, P., 2009.
**Impact of Diabetic Retinopathy**

Diabetic retinopathy is a major cause of visual impairment in the diabetic population. DR most commonly manifests as dark areas in the visual field or blurred vision.

**DR has serious impacts on patients’ vision, quality of life and costs**

In more advanced stages, DR can cause blurred vision, floaters and loss or change in perception of colour, and eventually spots in vision (see below right).

Prolonged DR can result in irreversible damage and permanent vision loss and blindness, with 2% of type 1 diabetic patients and 5% of type 2 diabetic patients progressing to blindness over 10 years.

Quality of life is greatly reduced as independence and mobility are limited with the loss of vision. DR patients incur substantially greater direct medical costs relative to diabetic patients without DR.

*Sources: Williams, 2004; Fryback et al, 1993; Lee et al. 2008; PharmaPoint, 2014; National Eye Institute, 2014*
Treatment of Diabetic Retinopathy

1970: Laser photocoagulation use in DR

1971: Laser, Vitrectomy, or no treatment

1980

1985: Vitrectomy in DR

1985

2017

2018

Laser has been and remains a key piece of the treatment paradigm for DR patients

Vitrectomy remains an option for those with most severe PDR

Injected intravitreallly (into the vitreous humour of the eye) once a month

Anti-VEGF intravitreal injection

Existing treatments focussing on one eye, requiring individual treatment of each eye

DR has a systemic cause and affects both eyes, oral treatment allows for simultaneous treatment of both

Sources: UptoDate
BI 1467335 currently investigated in two parallel Phase IIa trials

**Phase IIa PoCP in NASH patients**

*ClinicalTrials.gov Identifier: NCT03166735*
- Safety, Tolerability, PD, and PK in four doses
- N=108 from Europe and North America
- Initiated Aug 2017
- Study completion May 2019
- Sample size recently reduced by 27% due to improved assumptions on blinded baseline values

**Phase IIa PoCP in NPDR patients (ROBIN)**

*ClinicalTrials.gov Identifier: NCT03238963*
- Safety, Tolerability, PD, and PK with and without treatment
- N=100 from Europe and US
- Initiated Jan 2018
- Study completion Jan 2020
- Trial recently extended by 8 months due to slower than expected site initiation and recruitment
- Up to 25% additional sites overall added to best recruiting countries
### BI 1467335 next steps

<table>
<thead>
<tr>
<th>NASH</th>
<th>Diabetic Retinopathy</th>
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<tbody>
<tr>
<td>• Phase IIa results</td>
<td>• Phase IIa results</td>
</tr>
<tr>
<td>• Phase IIb trial in planning</td>
<td>• Phase IIb trial in planning</td>
</tr>
<tr>
<td>• Global pivotal Phase III trial(s) to follow in NASH patients with advanced fibrosis stages</td>
<td>• Global pivotal Phase III trial(s) to follow</td>
</tr>
<tr>
<td>• No proven regulatory pathway to date</td>
<td>• BI will closely interact with Regulators and Payers as development advances</td>
</tr>
<tr>
<td>• BI will closely interact with Regulators and Payers as development advances</td>
<td>• Current treatments are focussing on one eye only and systemic therapy such as BI 1467335 could address unmet medical need</td>
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<tr>
<td>• NASH is a multifactorial disease potentially requiring more than one MoA to show improvements</td>
<td>• BI 1467335 as early prevention of progression of DR could prevent invasive eye injections, operations and/or laser treatment which potentially result in loss of peripheral and night vision</td>
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<tr>
<td>• BI 1467335 could become an essential anti-inflammatory treatment for NASH patients</td>
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LOXL2/3 inhibitor program – A Competitive Profile

Dr Wolfgang Jarolimek
Pharmaxis Head of Drug Discovery
Genesis of fibrosis

- Metabolism
- Genetics
- Mechanical injury
- Chemicals

Activated cells

Collagen $\uparrow$

Lysyl oxidases $\uparrow$

Secreted collagen

Cross-linked collagen

Stiff matrix enhances inflammation and fibrosis
LOXL2 is a major player in organ fibrosis

LOXL2 is a diagnostic and prognostic biomarker for various fibrotic diseases

Emerging role of LOXL3

Comparative analysis of lysyl oxidase (like) family members in pulmonary fibrosis
Resolution of fibrosis

Inhibition of collagen and elastin cross links change existing fibrosis because of continuous re-modelling of tissue.

...liver collagen remodelling rates are higher in more advanced fibrotic disease—i.e., that the collagen pool in more fibrotic livers has a shorter half-life than in early disease.
Key Messages – Pharmacology

- **Existing data:**
  - **Liver fibrosis**
    - CCl₄-induced (Pharmalegacy, Shanghai); 6 wk mouse, 4 – 9 wks rat
    - Thioacetamide-induced (Pharmalegacy, Shanghai)
    - Stelic NASH model (SMC, Tokyo)
  - **Kidney fibrosis**
    - Diabetic nephropathy (Kolling Institute, Sydney)
    - eNOS-/ & db/db nephropathy (Vanderbilt Uni)
  - **Cardiac fibrosis**
    - Carotic aorta occlusion (CL Laboratory, Baltimore)
    - Ischemia/reperfusion (HRI, Sydney)
  - **Lung fibrosis**
    - Bleomycin-induced (Aragen, San Francisco)
    - Ad-TGF-β-induced (McMaster University, Toronto)
    - *In-vitro* fibroblastic focus model (Synairgen, UK)
  - **Cancer**
    - Oral cancer (Boston University)

- **Recent data:**
  - **Lung**
    - Repeated bleomycin-induced lung fibrosis model
  - **Liver**
    - Demonstrated changes in cross-links in human organoid model
**Bleomycin-induced lung fibrosis**

Bleomycin induced mouse lung fibrosis, prophylactic once a day oral gavage

Western blots and ELISA confirmed LOXL2 upregulation in the lung

LOXL2/3 inhibitors reduce LOXL2 activity in serum

=> Biomarker shows target engagement

Cross-links in the lung are reduced by LOXL2/3 inhibitors

=> Proof of mechanism in target tissue

Ashcroft score is reduced

=> Disease modification
Key Messages - Toxicology

IND safety package for C1 and C2

Both compounds successfully completed:
• 28 days toxicity in two species
• Cardiovascular study in dog
• Respiratory study in rat
• Behavioural study in rat
• In vitro (AMES and micronucleus) and in vivo micronucleus
• hERG

Preparation for Phase 2:
Both compounds successfully completed in life phase of 3 months tox studies in two species – Two NOAELs have been defined – awaiting histopathology of two studies

Toxicology studies to support entry into Phase 2 are well advanced
**Key Messages – Phase 1**

- **Double-blind placebo controlled Single Ascending Dose in healthy male volunteers**
  - Oral dosing of capsules
  - Safety, pharmacokinetics and pharmacodynamic measurements
  - C1
    - 10, 30, 60, 100, 200, 400 mg
  - C2
    - 5, 10, 20, 50, 100, 200 mg
  - Both compound were well tolerated at all doses, no safety signals detected
  - AUC and Cmax of both compounds increased with ascending dose; t₁/₂ ~22 hrs
  - Plasma LOXL2 was inhibited by >80% for 24 hrs after single dose

- **Double-blind placebo controlled Multiple Ascending Dose (14 days, once daily) in healthy male volunteers**
  - C1
    - 100, 200, 400 mg – human therapeutic dose based on LOXL2 inhibition is 400 mg once a day
  - C2
    - 50, 100, 200 mg – human therapeutic dose based on LOXL2 inhibition is 100 mg once a day
  - AUC and Cmax of both compounds increased with ascending dose and time. AUC and Cmax plateaued at Day 7 as predicted
  - Plasma LOXL2 was inhibited by >85% for 24 hrs after repeated once a day dosing
C1: PK - MAD

Dose-dependent increase in cmax and AUC. PK properties are as predicted from SAD data.
Target engagement in human

Repeated dosing resulted in >85% enzyme inhibition 24 hrs after last dose from Day 7 onwards. Human effective doses will be equal or below the above doses.
**Summary**

- **Overview**
  - C1 and C2 are mechanism-based full inhibitors of LOXL2 and LOXL3
  - Small molecules with favourable drug-like and developability profiles
  - Fast onset of inhibition
  - C1 and C2 have demonstrated the potential of LOXL2/3 inhibition as a truly anti-fibrotic treatment in many pre-clinical models and showed efficacy in combination therapy models
  - Target engagement can be determined in human, rat and mouse plasma/serum and rodent disease tissues
  - Once a day oral dosing
  - PK-PD and in vitro profiles allow for differentiation and positioning in multiple indications

- **Phase 1**
  - SAD and MAD for C1 and C2 have been completed with 108 healthy subjects on drug
  - C1 and C2 were well tolerated and no safety signals detected
  - AUC and Cmax of both compounds increased with ascending dose
  - C1 and C2 inhibited plasma LOXL2 at least 85% for 24 hrs after a single oral dose in MAD phase

- **Pre-clinical development**
  - C1 and C2 successfully finished in life phase of GLP 3-month tox studies in two species
  - Scalable synthetic routes and plan for production under cGMP available
  - Long term drug substance and formulation stability have been demonstrated
  - C1 and C2 are covered under separate patent applications with 2016 priority date
  - Target engagement assay has been filed under separate patent application with 2018 priority date
LOXL2/3 inhibitor program – Commercialisation

Gary Phillips
Pharmaxis CEO
## LOXL2 inhibitor program – value proposition

### approaching “deal ready” status

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<tr>
<th>Feature</th>
<th>What Pharma values</th>
<th>PXS program status</th>
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<td>Disease target</td>
<td>Independent validation</td>
<td>Multiple peer reviewed publications</td>
</tr>
<tr>
<td>Pre clinical proof of concept</td>
<td>2 or more different supportive animal models</td>
<td>Multiple supportive models across 5 different diseases. Target engagement linked to efficacy for first time</td>
</tr>
<tr>
<td>Dosing regimen</td>
<td>Ease of use</td>
<td>Oral once a day tablet or capsule</td>
</tr>
<tr>
<td>Patent</td>
<td>Composition of matter As long as possible</td>
<td>Composition of matter 2016 filing date; 100% PXS owned</td>
</tr>
<tr>
<td>Cost of Goods</td>
<td>Low</td>
<td>Small molecule with easy synthesis</td>
</tr>
<tr>
<td># Compounds</td>
<td>1 plus backups</td>
<td>2 compounds in clinical development plus back ups</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Wide therapeutic window As long as possible</td>
<td>28 day tox studies complete 13 week studies (2 species) 2 successfully completed; 2 in progress – report Q4 ’18</td>
</tr>
<tr>
<td>Clinical phase</td>
<td>Phase 1 with target engagement</td>
<td>Both compounds completed Phase 1</td>
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<tr>
<td>Target engagement</td>
<td>Drug inhibits target</td>
<td>&gt;85% inhibition for 24 hours from a single dose</td>
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**Phase 2 ready compounds now only one step away**
LOXL2 Commercialisation process

Negotiating from a position of strength

- Allow time to build scientific belief and credibility
- Generate competitive tension through transparency and continuous disclosure with multiple points of contact
- Looking for a partner with significant resources and clinical ambition in fibrosis.

Scientific Diligence  
Term Sheet negotiation  
Contract 1H 2019
Systemic pan LOX inhibitor program

Wolfgang Jarolimek
Pharmaxis Head of Drug Discovery
Lysyl oxidase family

- Lysyl oxidases are the major enzyme to cross-link collagen and elastin in any tissue
- Indications for systemic pan-LOX inhibitor is in very severe diseases and/or diseases with fast turnover of collagen and elastin
**Summary**

**Overview**
- PXS_LOXi is a mechanism-based full inhibitor of all lysyl oxidases
- Small molecule with favourable drug-like and developability profiles
- PXS_LOXi has demonstrated strong anti-fibrotic properties in pre-clinical models
- Target engagement can be determined in human, rat and mouse tissues
- Once a day oral dosing

**Pre-clinical development**
- IND-enabling studies successfully completed
  - 28 days toxicity in two species
  - Cardiovascular study in dog
  - Respiratory study in rat
  - Behavioural study in rat
  - In vitro (AMES and micronucleus) and in vivo micronucleus
  - hERG
- Systemic PXS_LOXLi are covered under separate patent application with 2018 priority date
**Target engagement**

**Pharmacokinetic properties of PXS_LOXi**

- Concentration of inhibitor is quickly decreasing after a single dose while inhibition of lysyl oxidase is long lasting.

**Pharmacodynamic properties of PXS_LOXi**

- Lysyl oxidase activity was measured in the skin of the ear which is a surrogate biomarker.
Pharmacology

Efficacious inhibitor in kidney fibrosis

**Model:** GATA-1 low Myelofibrosis model  
**Dose:** 15 mg/kg four times a week for 10 weeks

Efficacious inhibitor in Myelofibrosis

Bone marrow reticulum fibrosis
Next steps

1. Commence Phase 1 in healthy male volunteers (Q1 ‘19)
   a. Placebo controlled single ascending dose
   b. Placebo controlled multiple ascending dose
      • Readouts:
        • Safety
        • Pharmacokinetics
        • Pharmacodynamics, i.e., measuring the inhibition of lysyl oxidase activity
      => dose selection for 2.

2. Commence Phase 1 in patients (Q4 ‘19)
   a. Multiple dosing on top of standard of care
      • Readouts:
        • Safety
        • Pharmacokinetics
        • Pharmacodynamics, i.e., measuring the inhibition of lysyl oxidase activity
Fibrosis, LOX and Cancer

Dr Thomas Cox

Group Leader, Matrix and Metastasis, Cancer Division,
Garvan Institute of Medical Research
Targeting the Lysyl Oxidase (LOX) family in pancreatic cancer

Thomas R. Cox
Group Leader - Matrix and Metastasis
The Garvan Institute of Medical Research
and The Kinghorn Cancer Centre
Not-for-profit Medical Research Institute (MRI) established in Darlinghurst, Sydney in 1963.

Our Mission:

To make discoveries that enhance human health and society, leading to longer, healthier lives for everyone.

To achieve this Garvan unites over 600 of the most brilliant scientific minds in Australia, and is home to world-class cutting edge technology.

Garvan works across all majors diseases with research divisions in:

- Cancer
- Bone Biology
- Immunology
- Diabetes & Metabolism
- Neuroscience
- Genomics & Epigenetics.
Garvan has the unique capability to progress research all the way through to the patient in many diseases.

Long-running collaboration between two Sydney based partners: Garvan Institute and Pharmaxis.
Pancreatic Cancer as a highly aggressive disease

Approximately 3,200 new cases of pancreatic cancer annually in Australia and 450,000 worldwide.

In Australia alone, nearly 3,000 patients died of pancreatic cancer in 2017.

The median survival for untreated advanced pancreatic cancer is approximately 3-4 months.

The median survival for advanced pancreatic cancer, treated with our best therapeutics is currently only 6-8 months.
Pancreatic Cancer as a highly aggressive disease

Thus, the 5 year survival rate for pancreatic cancer is approximately 7-8%.

This statistic has barely improved in the last 25 years.

Pancreatic cancer therefore represents a significant economic burden of disease.

New treatments to improve outcome are seen as an urgent unmet clinical need.
Pancreatic Cancer as a highly aggressive disease

As pancreatic cancer progresses, an accompanying fibrotic response evolves within and around the developing tumour.

When tumours build this scar-like tissue in and around them, it decreases the efficacy of our therapies.

The scar-like (fibrotic) tissue does this by changing the tumour in several ways;

- Altering cancer cell behaviour, including making them more aggressive
- Directly and indirectly altering cancer cell sensitivity to therapies
- Acting as a physical barrier to the delivery of our adjuvant therapies
- Providing a highway for cancer cells to spread (metastasise) around the body
One of the major components of this scar-like tissue is fibrillar collagens.

The lysyl oxidases are critical in the production of these fibrillar collagens.

Opportunity to develop and deploy new therapies to co-target the development of this scar-like tissue in order to improve the efficacy of our already approved standard-of-care treatments.
The Lysyl Oxidase Family and Extracellular Matrix (ECM) in Cancer

i. Invasion/Migration
- Tumour-driven neoneurogenesis
- Cell-cell fusion
- Collective migration
- Re-seeding of primary tumour
- Tumour-driven lymphangiogenesis

ii. Intravasation
- Tumour-driven angio genesis
- CAF-mediated invasion
- Single-cell migration
- CTC clusters
- Shear stress

iii. Vessel transit/survival
- Lymphatic metastasis
- Transit of CAFs
- Neutrophil-mediated extravasation
- Platelet-CTC cross-talk

iv. Extravasation
- Dormant DTC-immune cell cross-talk
- Dormant DTC-microenvironment interaction
- Dormant to active DTC
- Dormant DTC-ECM-DTC interaction

v. Colonization
- Metastasis
- ECM-DTC interaction
- Stroma-DTC cross-talk
- CSC-initiated metastasis

Primary tumour priming of pre-metastatic niche
The Lysyl Oxidase (LOX) Family

~ The LOX family consists of 5 members (LOX, LOXL1, 2, 3 & 4).

~ Each member has the same catalytic domain.

~ This catalytic domain is critical to function.

~ Pharmaxis has developed a new LOX family inhibitor.

~ An oral once-a-day drug that inhibits all members.

~ My team is currently investigating the therapeutic potential of this compound in pancreatic cancer in combination with standard-of-care chemotherapy.

*Figure: Barker HE*, Cox TR* et al. *Nature Reviews Cancer* (2012)*

For personal use only
The LOX family in pancreatic cancer

~ All LOX family members are elevated in pancreatic cancer.

Targeting a single family member (LOX) has shown some success previously in combination with chemotherapy (Miller et al. *EMBO Mol. Med* (2015))

Our preliminary *in vivo* data targeting the whole LOX family using Pharmaxis’ new small molecule inhibitor has shown significant promise as a more robust approach to overcoming family member compensation and improving efficacy of standard of-care chemotherapy.

Data from Miller et al. *EMBO Mol. Med* (2015) - Kaplan-Meier analyses showing correlation of LOX family member expression and survival in the Glasgow patient cohort (microarray analysis of 400 cores from a total of 80 PDAC resections)
A unique local opportunity for trial implementation.

Clinical Trials Unit (CTU) at The Kinghorn Cancer Centre (TKCC) has a dedicated Phase I unit.

Currently running approximately 18 Phase I trials and over 200 trials across all Phases.

Key strength is the close integration of over 250 clinicians and researchers under one roof.

Bench to bedside (and back again)
Summary

The scar-like (fibrotic) tissue changes that accompany pancreatic tumour development are known to play a significant role in the poor outcome and poor survival of patients.

Lysyl oxidases are crucial to the formation of this scar-like (fibrotic) tissue.

Pharmaxis’ new compound which targets the whole lysyl oxidase family offers the potential to block the formation of this scar-like (fibrotic) tissue in tumours.

By blocking the formation of this scar-like (fibrotic) tissue we may be able to boost the efficacy of current standard-of-care chemotherapy treatments and improve outcome and survival for pancreatic cancer patients.
Pharmaxis Business Strategy

Gary Phillips
Pharmaxis CEO
Pharmaxis has a successful track record of research, development and commercialisation of human healthcare products for the treatment and management of fibrotic and inflammatory diseases.

**Value Generation**
- Extensive Big Pharma network
- Seek to partner after phase 2 to realise value and mitigate program and corporate risk

**Drug Discovery Engine**
- Leverage small molecule expertise and in house chemistry platform
- Efficiencies from global academic & CRO networks
- Target high value diseases with validated targets

**Clinical Trials**
- Utilise global experience and extensive clinical networks to execute value adding Phase 2 clinical trials

**Value Generation**
- Extensive Big Pharma network
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