R&D Showcase Webinars
Pharmaxis drug PXS-5505 targeting several cancers
Forward looking statement

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<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
<th>Speaker(s)</th>
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<tbody>
<tr>
<td>11.00</td>
<td>Welcome and introduction to program</td>
<td>Michael Woods</td>
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<tr>
<td>11.05</td>
<td>Introduction to Pharmaxis research and clinical development program</td>
<td>Dr Wolfgang Jarolimek&lt;br&gt;Gary Phillips</td>
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<tr>
<td>11.15</td>
<td>The myelofibrosis landscape and MF-101</td>
<td>Dr Gabriela Hobbs (Massachusetts General Hospital)</td>
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<td>11.45</td>
<td>Hepatocellular cancer and Rochester University investigator led study</td>
<td>Dr Paul Burchard (Rochester NY)</td>
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<td>12.15</td>
<td>Pancreatic Cancer</td>
<td>Dr Tom Cox (Garvan Sydney)</td>
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<td>12.40</td>
<td>Pharmaxis Q&amp;A</td>
<td>Gary Phillips</td>
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<td>13.00</td>
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<tr>
<td>Pharmaxis’ portfolio of compounds in research and development</td>
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<td>**</td>
<td><strong>Pre-clinical</strong></td>
<td><strong>Phase 1</strong></td>
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<tr>
<td><strong>PXS-5505</strong> Pan-LOX Inhibitor</td>
<td>Myelofibrosis</td>
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<td></td>
<td>Myelodysplastic syndrome</td>
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<td></td>
<td>Hepatocellular carcinoma</td>
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<td></td>
<td>Fibrotic diseases/other cancer</td>
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<tr>
<td><strong>PXS-6302</strong> Pan LOX inhibitor</td>
<td>Established scars</td>
<td></td>
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<td></td>
<td>Post surgical burns scarring</td>
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<tr>
<td><strong>PXS-4728</strong> SSAO Inhibitor</td>
<td>Neuroinflammation</td>
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<tr>
<td><strong>PXS-5382</strong> LOXL2 Inhibitor</td>
<td>Idiopathic pulmonary fibrosis</td>
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<td></td>
<td>Kidney fibrosis</td>
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<tr>
<td><strong>PXS-5370</strong> SSAO/MPO Inhibitor</td>
<td>Lung inflammation</td>
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<tr>
<td><strong>PXS-4699</strong> SSAO/MAO-B Inhibitor</td>
<td>Organ fibrosis and inflammation</td>
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<td></td>
<td>Enzyme Inhibitor</td>
<td>Inflammation</td>
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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

**PXS-5505**
- Oral dosage form – twice a day dosing
- 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

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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
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
## Four trials to deliver near term value

Pipeline creates multiple opportunities in high value markets

<table>
<thead>
<tr>
<th>Indication</th>
<th>Addressable market (US$)</th>
<th>Trial design</th>
<th># patients</th>
<th>Status</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelofibrosis (MF)</td>
<td>$1 billion</td>
<td>Phase 2 open label 6 month study in JAK intolerant / ineligible myelofibrosis patients</td>
<td>24</td>
<td>Recruiting</td>
<td>Year end 2022</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma (HCC)</td>
<td>$7 billion</td>
<td>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)</td>
<td>18</td>
<td>First Patient Q2 2022</td>
<td>2H 2023</td>
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<tr>
<td>Modification of established scars</td>
<td>$3.5 billion</td>
<td>Phase 1c 3 month placebo controlled study in patients with established scars (&gt;1 year old)</td>
<td>50</td>
<td>Recruiting</td>
<td>Q4 2022</td>
</tr>
<tr>
<td>Scar prevention post surgery</td>
<td>$3.5 billion</td>
<td>Phase 1c 3 month placebo controlled study in patients with scarring subsequent to a burns injury</td>
<td>50</td>
<td>First patient mid 2022</td>
<td>1H 2023</td>
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The myelofibrosis landscape and MF-101
Dr Gabriela Hobbs (MGH)
MYELOFIBROSIS TREATMENT LANDSCAPE
Outline

• What is myelofibrosis?
• Current treatment landscape
• Drugs in development
• Rationale for LOX inhibition in MF
Myelofibrosis

1.8-7 year survival

Overall Survival (probability)

Years
Myelofibrosis epidemiology in the USA

<table>
<thead>
<tr>
<th>18,000 people live with MF</th>
<th>Average age at diagnosis- 65</th>
<th>30% transform to leukemia</th>
<th>Most patients live with significant symptoms</th>
</tr>
</thead>
</table>

12
Mutations in myelofibrosis

- **Triple negative patients**: 8% ET and MF

- **JAK2 V617F**: 50-60% ET and MF, >95% of PV

- **CALR**: 20-30% of ET and MF

- **MPL**: 5-7%

**Mutations in myelofibrosis**

- Mutant CALR binds MPL in the endoplasmic reticulin
Myelofibrosis Treatment Approach

- **Very Low Risk**: Observation
- **Low Risk**: Needs therapy?
  - Symptoms Bothersome spleen: JAK inhibitors (ruxolitinib, fedratinib, pacritinib)
- **Intermediate Risk**: Needs therapy?
- **High and Very High Risk**: Transplant candidate?

Transplant Clinical Trial
Myelofibrosis approach summary

- **Myelofibrosis**
- **Low risk** = Observation
- **Low blood counts** = Limited options
- **New Treatments Needed**
- **Curative therapy? Transplant**
- Transplant ineligible? Very poor outcome
## JAK Inhibitors - Pros and Cons

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td>Symptom improvement</td>
<td>Decreased blood counts</td>
</tr>
<tr>
<td>Spleen size reduction</td>
<td>Does not alter disease progression</td>
</tr>
<tr>
<td>? Survival benefit</td>
<td>Response will eventually be lost</td>
</tr>
<tr>
<td>Improved quality of life</td>
<td>Outcome after Jakafi failure is poor</td>
</tr>
<tr>
<td>Agents</td>
<td>Class of drug</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Palabresib + Rux</td>
<td>BETi</td>
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<tr>
<td>Navitoclax + Rux</td>
<td>BCL2i</td>
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<tr>
<td>Parsaclisib + Rux</td>
<td>P13Kd</td>
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<tr>
<td>Luspatercept + Rux</td>
<td>ActRII ligand trap</td>
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<tr>
<td>Pacritinib</td>
<td>JAKi/IRAK1</td>
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<td>Jaktinib</td>
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<td>Momelotinib</td>
<td>JAKi</td>
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<tr>
<td>Fedratinib</td>
<td>JAKi</td>
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<tr>
<td>Imetelstat</td>
<td>Telomerase inh.</td>
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The role of lysyl oxidase in Myelofibrosis

- Lysyl oxidases- important to making scar tissue
- There are 5 LOX enzymes in mammals
- In MF there is elevated expression of most of the LOX enzymes
- PX5-5505 is a pan-LOX inhibitor that is well tolerated without off-target activities (as seen in other LOX inhibitors)
LOX in Myelofibrosis

ECM: extracellular matrix
EPOR: erythropoietin receptor
JAK: janus kinase
MK: megakaryocyte
PDGFR: platelet-derived growth factor receptor
SC: stem cell
STAT: signal transducer and activator of transcription

Inflammation ↑
MK and SC proliferation ↑
ECM protein ↑
Hematopoiesis ↓

PXS-5505 effects in animal models

Clinical manifestations
Cytopenia
Splenomegaly
MK dysplasia

Vicious circle of disease progression
Mechanical stress
Activation
Fibrosis
Matrix stabilising elastin and collagen cross-links
Extracellular matrix - reticulin
Pan-LOX inhibitor
PXS-5505

Piasecki et al Arch Stem Cell 2021
Pan-LOX inhibition in MF

• The central hypothesis:

Effective inhibition of LOX will prevent collagen cross-linking, reduce marrow fibrosis and allow normal hematopoiesis to resume. Normal hematopoiesis will result in normalization of blood counts and reduction in spleen size.
PX5-5505 experience - Safe and effective LOX inhibitor

PX5-5505 attenuates hallmarks of primary myelofibrosis

in mice

- Phase 1c dose escalation in MF patients
- Dose 1
- Dose 2
- Dose 3

PX5-5505 – Maximum of 3 patients on each dose for 28 days
- Open label dose expansion in JAK-inhibitor unsuitable primary MF or post-ET/PV MF patients
- 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
**PXS-5505 Phase 1/2a Trial in myelofibrosis**

6 month monotherapy study with meaningful safety and efficacy endpoints (phase 1c complete)

<table>
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<tr>
<th>STUDY POPULATION</th>
<th>DESIGN</th>
<th>TREATMENT COHORT</th>
<th>ENDPOINTS</th>
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</table>
| 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 | Phase 1/2a open label study to evaluate safety, PK/PD, and efficacy | Dose escalation: PXS-5505  
3 ascending doses, 4 weeks  
(n = 3 to 6 subjects/dose) | Primary: Safety TEAEs  
Secondary: PK/PD  
BMF Grade  
IWG Response  
SVR  
Haematology  
Symptom score |
| Multiple sites across 4 countries to enhance trial recruitment (USA, South Korea, Taiwan, Australia) | Study budget (~US$6m) | Study recruitment commenced Q1 2021, study targeted to conclude H2 2022 |

*Unsuitable = ineligible for JAKi treatment, intolerant of JAKi treatment, relapsed during JAKi treatment, or refractory to JAKi treatment. JAKi – Janus Kinase inhibitor, MF myelofibrosis, ET Essential Thrombocythaemia, PV polycythaemia vera, INT intermediate, BMF bone marrow fibrosis, RP2D recommended phase 2 dose, TEAE treatment emergent adverse event, PK pharmacokinetics, PD pharmacodynamics, SVR spleen volume response, IWG International Working Group Myeloproliferative Neoplasms

FDA granted orphan drug designation July 20 and IND approved August 2020

**STUDY POPULATION**

- 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

**DESIGN**

- Phase 1/2a open label study to evaluate safety, PK/PD, and efficacy

**TREATMENT COHORT**

- Dose escalation: PXS-5505
  - 3 ascending doses, 4 weeks
  - (n = 3 to 6 subjects/dose)

**ENDPOINTS**

- Primary: Safety TEAEs
- Secondary: PK/PD
  - BMF Grade
  - IWG Response
  - SVR
  - Haematology
  - Symptom score

Studies budget (~US$6m)

Study recruitment commenced Q1 2021, study targeted to conclude H2 2022
Thank you
Hepatocellular cancer and Rochester University IIS
Dr Paul Burchard (Rochester NY)
A Phase 1b/2 Trial of PXS-5505 Combined With First Line Atezolizumab plus Bevacizumab For Treating Patients With Unresectable Hepatocellular Carcinoma
Primary liver cancer incidence and deaths U.S.

Source: SEER Cancer Statistic Database, U.S. DHHS
Resectability & Current Treatment Options

- Only 20-30% of cases resectable at presentation
- Sorafenib initial 1st line therapy

Llovet et al. NEJM 2008
Resectability & Current Treatment Options

- **HIMALAYA**: Durvalumab (Anti-PDL1) & Tremelimunab (Anti-CTLA4)
- **IMBRAVE50**: Atezolizumab (Anti-PDL1) & Bevacizumab (Anti-VEGF) combination therapy now 1st line
- Replacing Sorafenib at many institutions

Finn et al. NEJM 2020
Lysyl Oxidase (LOX)

Conventional mechanisms of LOXs

- LOX
- LOXL1
- LOXL2
- LOXL3
- LOXL4

Normal tissue

Collagen

Tumour with fibrotic tissue has
- increased tissue stiffness
- increased interstitial pressure

Increased EMT

Increased invasion

Increased tumour growth

Decreased drug perfusion

Increased angiogenesis
LOX is associated with poor outcomes in HCC

LOX expression is associated with HCC metastases and recurrence

Gene expression HCC

Recurrence & Survival

Umezaki et al. Cancer Science, 2019
LOXL2 promotes HCC intrahepatic metastases and local invasion

LOX inhibition disrupts tumor stroma & improves drug delivery:

Le Calve et al., *Oncotarget* 2015, Miller et al., *EMBO Mol Med* 2018
Combination Therapy with PXS-5505 Delays Tumor Progression and Improves Survival in a Murine Model of Primary Liver Malignancy

Tumor Growth

Ascites Onset

Survival

\[ p < 0.0001 \]
\[ p = 0.0026 \]
\[ p = 0.001 \]
PXS-5505 in Primary Liver Malignancy

**Oral Presentations**
- Americas Hepato-Pancreatico-Biliary Association, 2021
- Society of Surgical Oncology, 2022
- International Hepato-Pancreatico-Biliary Association, World Congress, 2022

**Poster Presentations**
- American Association for the Study of Liver Diseases, 2021
- American Association for Cancer Research, Advances in Pathogenesis and Molecular Therapies of Liver Cancer, 2022
Phase 1b/II Trial Design: Unresectable &/or Non-Transplantable HCC

FDA Approval of IND – September 2021
Anticipated Enrollment – May/June 2022

Phase Ib Cohort
18 Patients

Timeline
1. 43-day total interphase
2. Assessment of dose tolerability at 3 week intervals
3. Biopsy for correlative science prior to treatment initiation and at conclusion
4. CT imaging per routine guidelines to assess response (2-3mo)
5. pK lab draws for analysis days 1, 22, 43

Phase II Cohort
1. Designed for objective response rate of 45%
2. Anticipate 12 patients at MTD in Phase Ib to determine rationale for expansion to Phase II study
3. Would require 4 patients at MTD to demonstrate response in order to proceed
4. Phase II expansion for total of 42 patients at MTD
Phase 1 Trial Design: Unresectable &/or Non-Transplantable HCC

**Inclusion Criteria**
- Unresectable, not transplant candidate (incl. metastatic)
- ≤ Child A cirrhosis
- ECOG 0 or 1
- Meets criteria for 1st line therapy
- Cross-sectional imaging prior to enrollment

**Exclusion Criteria**
- Connective tissue disorder
- Evidence of aneurysmal disease
- Known of suspected autoimmune disease
- History of myelodysplastic or myeloproliferative disorders
- Major surgery within 4 weeks of enrollment

**Escalation/De-escalation Schema**

<table>
<thead>
<tr>
<th>Group</th>
<th>Atezolizumab</th>
<th>Bevacizumab</th>
<th>PXS-5905</th>
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<tbody>
<tr>
<td>1</td>
<td>1200mg every 3 weeks</td>
<td>15mg/kg every 3 weeks</td>
<td>100mg BID</td>
</tr>
<tr>
<td>2</td>
<td>1200mg every 3 weeks</td>
<td>15mg/kg every 3 weeks</td>
<td>150mg BID</td>
</tr>
<tr>
<td>3</td>
<td>1200mg every 3 weeks</td>
<td>15mg/kg every 3 weeks</td>
<td>200mg BID</td>
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Phase 1 Trial Design: Unresectable &/or Non-Transplantable HCC

Enrollment & Consent

Baseline PK Draw Day 1

PK Draw Day 22

PK Draw Day 43

43 Day interphase

Imaging &/or Bx consistent with Unresectable &/or non-transplantable HCC

Pre-Rx Biopsy*

Study Dose

Baseline

PK Draw

Day 1

PK Draw

Day 22

PK Draw

Day 43

8-12wks CT scan +/- Biopsy*

Biopsy analysis

IHC

RNA

Flow Cytometry

*Biopsy not standard of care
Phase 1 Trial Design: Unresectable &/or Non-Transplantable HCC

Baseline
PK Draw Day 1

43 Day Interphase

PK Draw Day 22

PK Draw Day 43

Enroll next 2 eligible patients

Dose safety determination

HCC

3 weeks

PXS-5505 + Atezolizumab + Bevacizumab

3 weeks

PXS-5505 + Atezolizumab + Bevacizumab

Continue regimen until surveillance CT

Day 1

Day 22

Day 43

Baseline PK Draw Day 1

PK Draw Day 22

PK Draw Day 43

43 Day interphase

Enroll next 2 eligible patients

Dose safety determination

HCC

3 weeks

PXS-5505 + Atezolizumab + Bevacizumab

3 weeks

PXS-5505 + Atezolizumab + Bevacizumab

Continue regimen until surveillance CT
Phase 1b: Enrollment begins at dose 0, and proceeds by BION rules dependent on observed rates of DLT, target DLT rate 0.3.

Patients enroll via Bayesian Optimal Interval Design (BOIN). Model detects Maximal Tolerated Dose (MTD) with a target DLT rate of 0.3. All patients evaluated for secondary endpoints.

Patients continue to enroll via BOIN rules until n=12 patients have been enrolled to a single dose yielding a 0.3 DLT rate.

After 12 patients enroll and are evaluated for RECIST 1.1 at MTD, evaluation of futility based on Two Stage Design occurs in this population.

Simon’s Two Stage Rules:
- \( \leq 3 \) responses: Do not expand into Phase 2 cohort given futility.
- \( >3 \) responses: Begin Phase 2 expansion cohort, with 30 additional patients at MTD (n=42 total patients).

Phase 2: Accrual continues in Phase 1b until the 12th patient is evaluated for RECIST 1.1. Phase 2 Enrollment begins once 12th evaluation passes Simon’s Two Stage Rule. Total number of patients between Phase 1b/2: n=42-48, but expected to be 48.
Thank You
Pancreatic Cancer
Dr Tom Cox
Garvan Institute (Sydney)
Targeting the Lysyl Oxidases in Pancreatic Cancer

R&D Briefing; PXS-5505 - 29th March 2022

A/Prof Thomas R. Cox
Laboratory Head - Matrix and Metastasis, Garvan Institute of Medical Research
Our Mission:

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

Garvan works across all major diseases with research programs in:

- Cellular Science
- Genomic Science
- Translational Science
- Data Science

700 research partners and collaborators globally
Garvan through its integration with St Vincents Hospital Precinct has the unique capability to progress research all the way through to the patient in many diseases, especially cancer.
The Extracellular Matrix (ECM) or ‘matrix’

Cells are the basic building block of life

Extracellular Matrix

Collagen I / Neutrophils
The matrix perspective in solid tumours

The extracellular matrix plays a fundamental role in all tissues to maintain normal function

The vast complexity of the extracellular matrix contributes across a variety of time and length scales to modulate cell behaviour on an ongoing basis

It is typically highly dysregulated in cancer and is important in the progression of solid tumours as well as the modulation of tumour response to therapy

Cox TR (2021) *Nature Reviews Cancer*
Pancreatic Ductal Adenocarcinoma as a highly aggressive disease

- **3,000** deaths in Australia in 2019
- **5-year** probability of survival: **9%**
- **Highly Fibrotic** nature
- Chemotherapy is the mainstay of patient treatment

AIHW 2019 - Cancer In Australia
Pancreatic Ductal Adenocarcinoma as a highly aggressive disease

- 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 6-8 months
- This statistic has barely improved in the last 2-3 decades
- Pancreatic cancer therefore represents a significant economic burden of disease
- New treatments to improve outcome are seen as an urgent unmet clinical need
Pancreatic tumours contain high levels of fibrosis (desmoplasia)

As pancreatic cancer progresses, an accompanying fibrotic response (desmoplasia) evolves within and around the developing tumour. As this scar-like tissue builds up, it decreases the efficacy of our standard-of-care therapies.

Polarised light microscopy allows visualisation of fibrillar collagens, the major component of tissue fibrosis.
Pancreatic tumours contain high levels of fibrosis (desmoplasia)

PicRed Birefringence

Polarised light microscopy

Tumour fibrosis drives disease progression by...

- 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 physical highway for cancer cells to spread (metastasise) to other parts of the body
Drivers of tumour fibrosis (desmoplasia)

- Prominent pathological characteristic of pancreatic cancer, marked by a significant overproduction of extracellular matrix and extensive proliferation of “Cancer Associated Fibroblasts” (CAFs)

- Occurs at primary and secondary sites

- Driven by multiple intercellular and intracellular biological signalling events (including, but not limited to, growth factors such as PDGF, TGFβ, FGFs, TNF-α, CTGF, IL-1β)

- Desmoplasia feeds back to activate intracellular signalling programs inside cancer cells driving progression in a process known as “Dynamic Reciprocity”

- Therefore, targeting the deposition of matrix offers a powerful approach to break this cycle

Setargew YSI, Wyllie K, Grant RD, Chitty JL & Cox TR (2021) Cancers
The Lysyl Oxidase (LOX) family in tumour fibrosis

- One of the major components of tumour desmoplasia is fibrillar collagens

- The lysyl oxidase enzymes (LOX, LOXL1, LOXL2, LOXL3 and LOXL4) are the critical linchpin in the production of fibrillar collagens through enabling their assembly and cross linking

- Opportunity to develop and deploy new therapeutic approaches to co-target the development of this scar-like tissue in order to improve the efficacy of our already approved standard-of-care treatments

Each of the lysyl oxidase family members are up-regulated in pancreatic ductal adenocarcinoma (PDAC) and individually associated with poor survival.

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) - Miller et al. EMBO Mol Med.
Further analysis in two additional patient cohorts (TCGA and APGI/ICGC) reveals that a combination score encompassing expression of all 5 family members is significantly associated with survival.

A low family score (light blue) is associated with an approximately 2 fold increase in patient median survival.

**Chitty et al. Nature Cancer (in revision)**
Pre-clinical models of pancreatic ductal adenocarcinoma

The “KPC” mouse model of spontaneous pancreatic cancer, along with human patient derived xenograft (PDX) models (part of the Australian APGI and APMA programs) develop robust tumour desmoplasia allowing for detailed characterisation of novel anti-fibrotic compounds.

\( Pdx-1-Cre \; LSL-Kras^{G12D/+} \; LSL-tp53^{R172H/+} \) (KPC)

Patient derived xenograft (PDX) models

https://www.pancreaticcancer.net.au/apma/

https://www.pancreaticcancer.net.au/apga/

Australian Pancreatic Cancer Genome Initiative

https://www.pancreaticcancer.net.au
Pre-clinical evaluation of PXS-5505 in combination with standard-of-care chemotherapy (gemcitabine) in genetically engineered mouse (KPC), and human patient derived xenograft (PDX) models of pancreatic cancer.

Chitty et al. *Nature Cancer* (in revision)
PXS-5505 in combination with standard-of-care gemcitabine

~ Decreased tumour growth leading to increased median survival over chemotherapy alone

~~ Median Survival: **85** days

~~ Median Survival: **125** days

~~ Median Survival: **171** days

~ Decreased tumour desmoplasia (fibrosis)

~ Decreased metastatic burden in the liver

Chitty *et al.* Nature Cancer (in revision)
Summary

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

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

Therapies that target this deposition, such as through targeting the lysyl oxidases, offer a way to block cumulative tumour desmoplasia, and augment the efficacy of current standard-of-care therapies.

Our pre-clinical data using PXS-5505 in combination with standard of care chemotherapy in mouse and human models of pancreatic cancer demonstrate improved survival supporting future translation into Phase II clinical trials.
developing breakthrough treatments for fibrosis and inflammation

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