

**ASX RELEASE**

**11 February 2021**

**Investor Update**

Amplia Therapeutics Limited (ASX: ATX) (“Amplia” or the “Company”) is pleased to provide the attached Investor Update.

This ASX announcement has been authorised for release by the Board.

- End -

**For Further Information**

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**About Amplia Therapeutics Limited**

Amplia Therapeutics Limited is an Australian pharmaceutical company advancing a pipeline of Focal Adhesion Kinase (FAK) inhibitors for cancer and fibrosis. FAK is an increasingly important target in the field of cancer immunology and Amplia has a particular development focus in pancreatic and ovarian cancer. FAK also plays a significant role in a number of chronic diseases, such as idiopathic pulmonary fibrosis (IPF).

# Amplia Therapeutics Investor Update

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February 2021

Amplia Therapeutics Limited



# Disclaimer

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There can be no assurance or guarantee that actual outcomes will not differ materially from these statements. The data and results pertaining to clinical subjects used in this presentation are illustrative of medical conditions and outcomes associated with potential applications of Amplia’s acquired product pipeline. Actual results from clinical trials may vary from those shown.

# Company highlights



- Developing small molecule drugs against Focal Adhesion Kinase (FAK) for two, significant disease areas
  - **cancer**
  - **fibrosis**
- Range of commercial opportunities for partnering, licensing and co-development
- Capital raised in July 2020 to fund Phase 1 trial, preclinical studies and to provide working capital
- Phase 1 clinical trial on track to complete in Q2 2021
  - Data from Phase 1 trial expected to support further clinical studies in multiple cancer and fibrotic disease indications
- Phase 2 clinical trial program targeted in 2021



# Company snapshot <sup>1</sup>



Shares on issue	107.7M
Market capitalization - undiluted	\$29.9M
Options on issue	13.9M
Cash <sup>2</sup>	\$2.8M

Headquarters Melbourne

Board  
 Warwick Tong (Chair)  
 John Lambert (MD)  
 Robert Peach (NED)  
 Chris Burns (NED)

Substantial institutional holders  
 Platinum – 16.2%  
 Blueflag Holdings – 7.1%

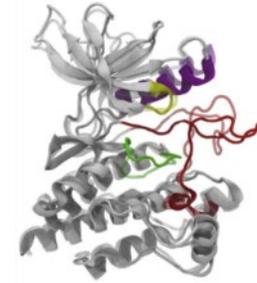


Price <sup>1</sup>	\$0.27
12mth high - low	\$0.37 - \$0.04
4wk av. daily volume	168,000

<sup>1</sup> as at close of trade, 9 Feb 2021

<sup>2</sup> As at 31 Dec 2020

# Focal Adhesion Kinase – dual purpose drug target



## Cancer

- Cell migration and metastasis
- Collagen accumulation
- Local regulation of immune response

## Fibrosis

- Collagen accumulation
- Fibronectin production

## Biology

## Commercial Opportunity

### Combination Therapy

- Pancreatic cancer
- Ovarian cancer

### Monotherapy

- Lung fibrosis
- Liver fibrosis
- Ocular fibrosis

# Amplia is developing two FAK inhibitors

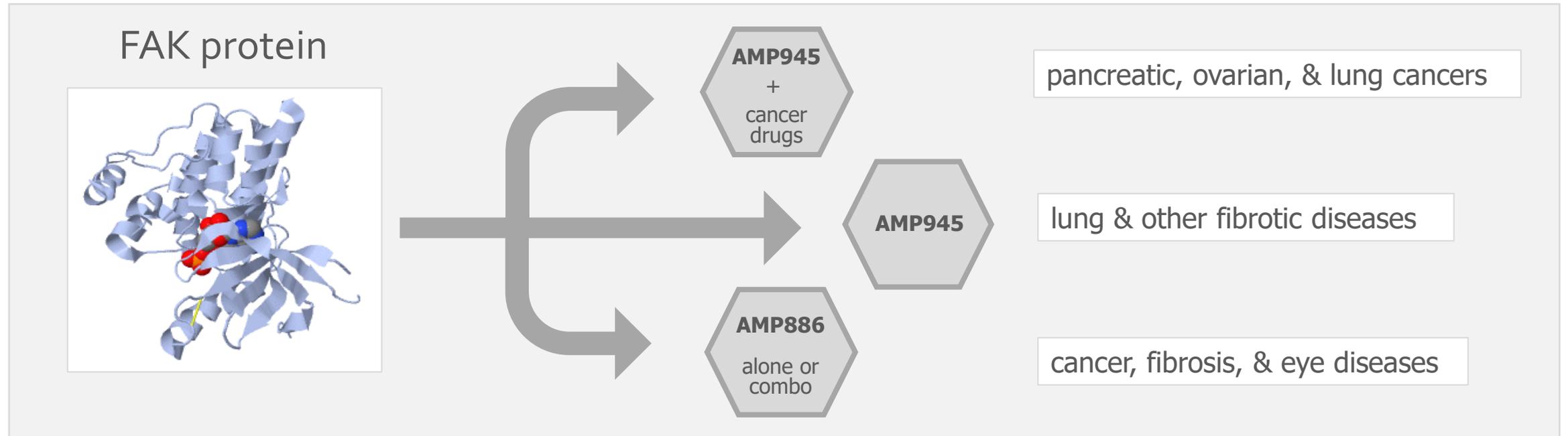


Amplia has exclusive, worldwide licenses to two proprietary, FAK inhibitors:

- **AMP945** – highly potent, highly selective, orally bioavailable – only blocks the FAK protein
- **AMP886** – orally bioavailable, potent blocker of the FAK protein and other cancer drug targets

Both were developed by the Cancer Therapeutics CRC (CTx) – a collaboration of Australia’s leading cancer researchers whose past commercial successes include:

- licensing a drug to Merck in 2016 (US\$15M upfront, up to US\$500M milestones + royalties)
- establishing a collaboration and license agreement with Pfizer in 2018 (US\$14M upfront, up to \$US460M milestones + royalties)

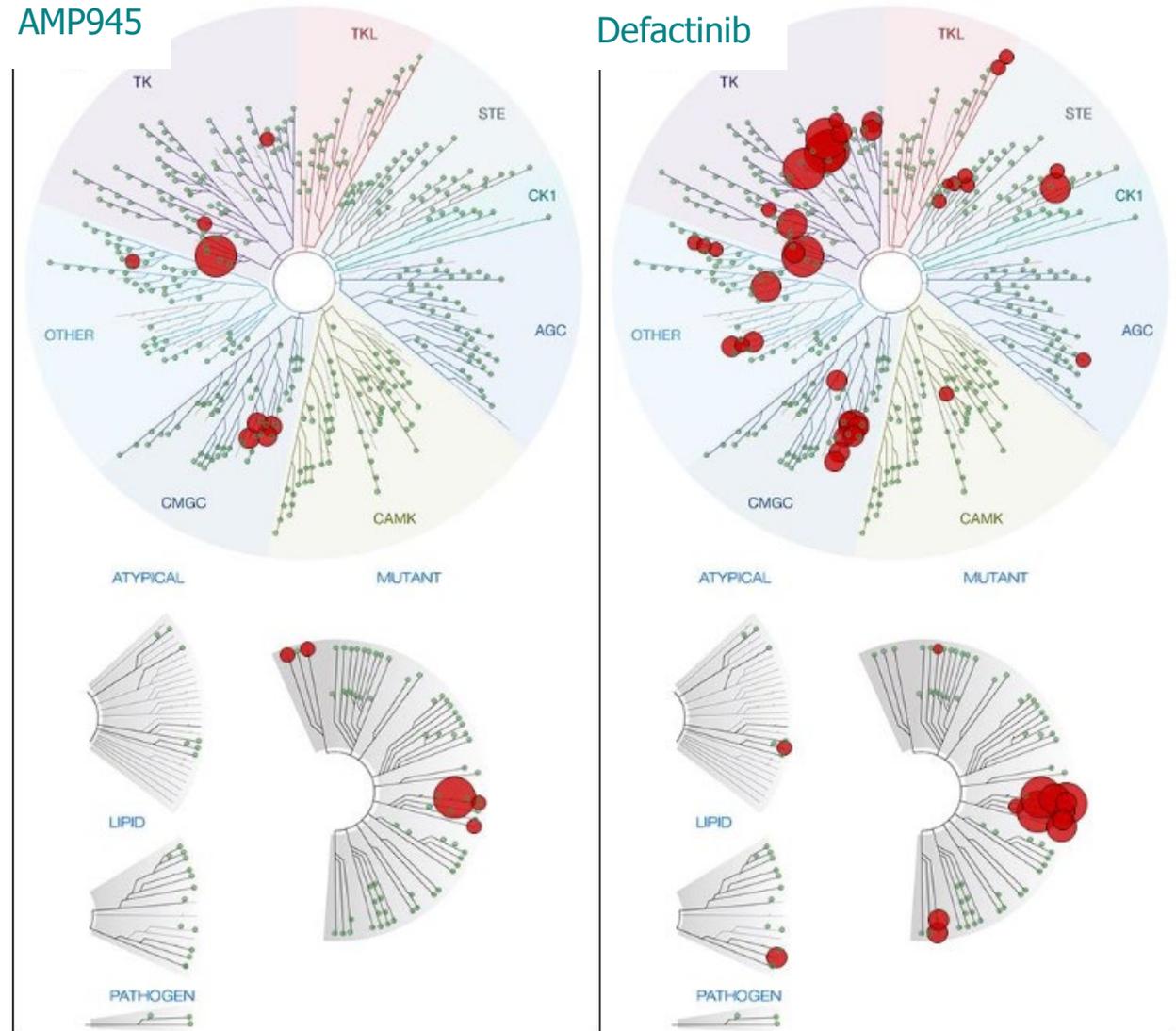


# AMP945 is highly selective for FAK



Non-specific kinase inhibition often leads to clinical side effects

- 468 kinases screened at a concentration of 1 $\mu$ M
- AMP945 shows improved selectivity compared to competitor agents – e.g. defactinib



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# Cancer treatments

# Why cancer drugs often do not work

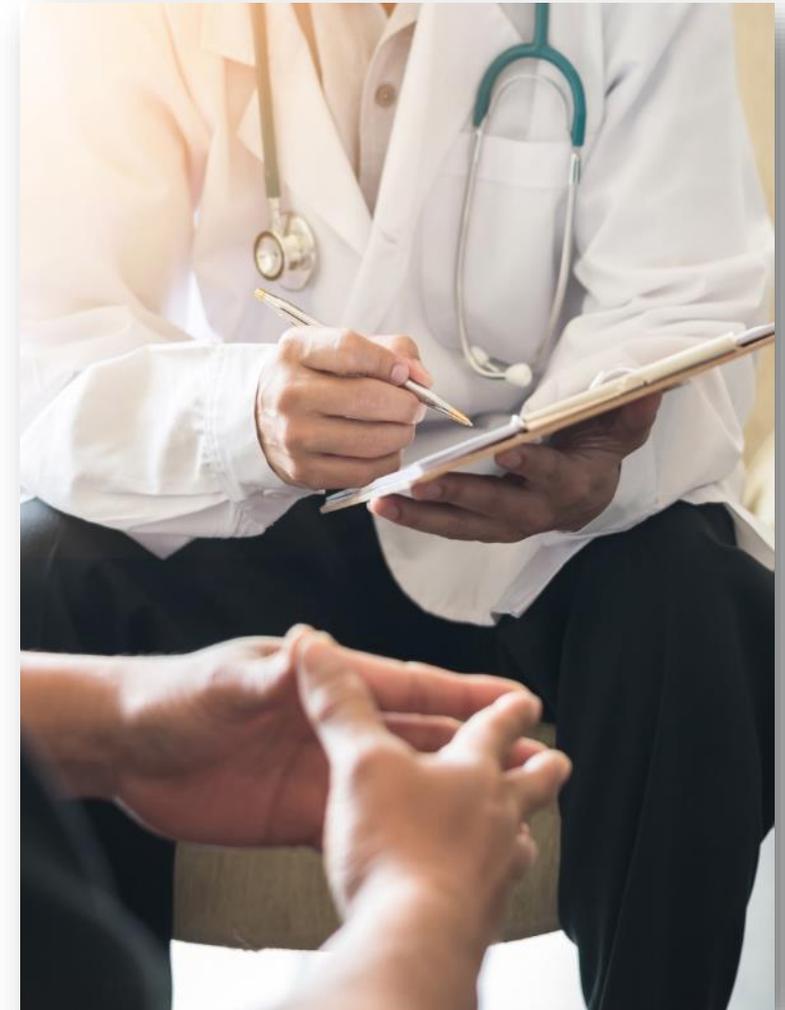


Pharmaceutical strategies to treat cancer:

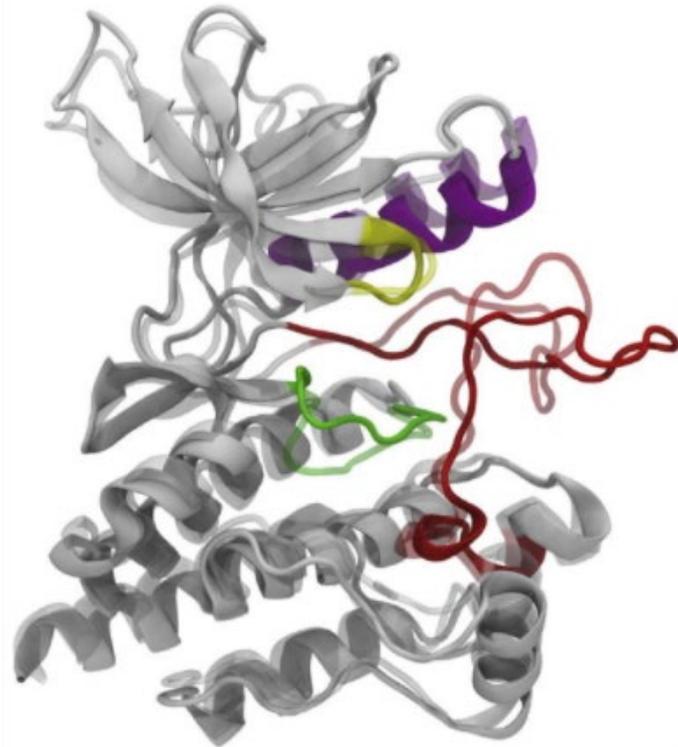
1. **cytotoxic drugs:** target rapidly dividing cancer cells
2. **targeted drugs:** block specific proteins elevated in cancer cells
3. **anti-angiogenic drugs:** block new blood vessels which feed the cancer
4. **immuno-oncology (I-O) drugs:** activate the immune system to attack the cancer

The effectiveness of these is drugs limited by tumour 'defence' mechanisms which:

- allow cancers to spread to other sites in the body
- generate resistant cancer cells
- physically shield the cancer from the immune system
- dampen the immune system's response against the cancer



# Targeting cancer's defence mechanisms



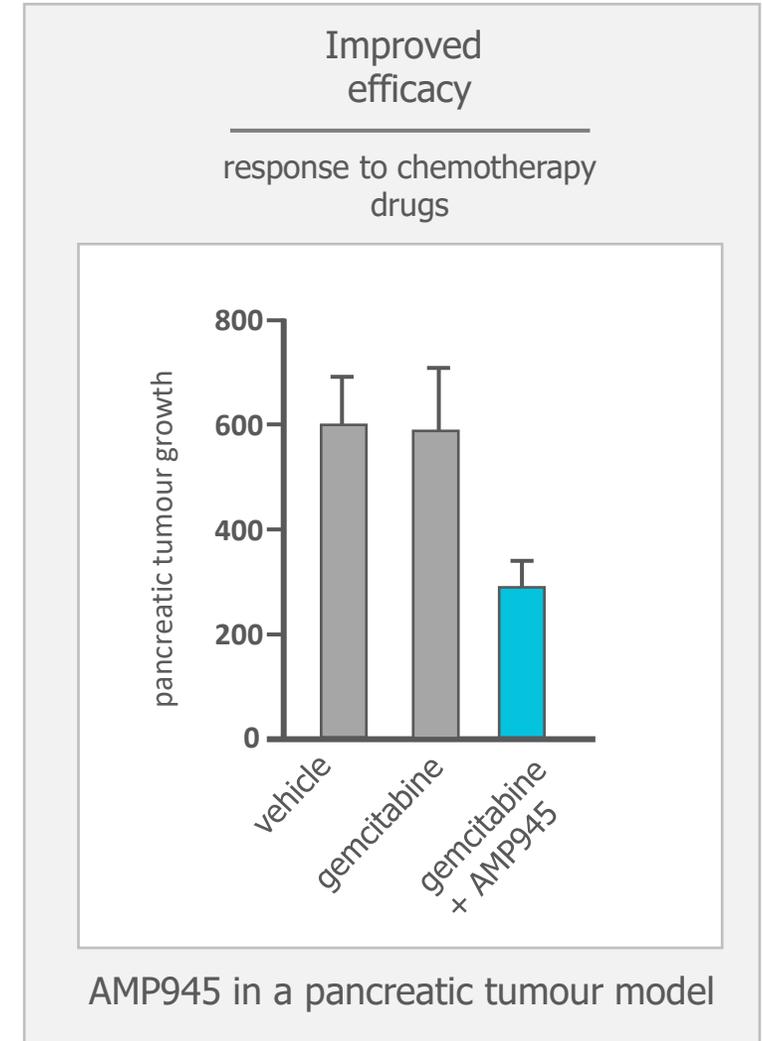
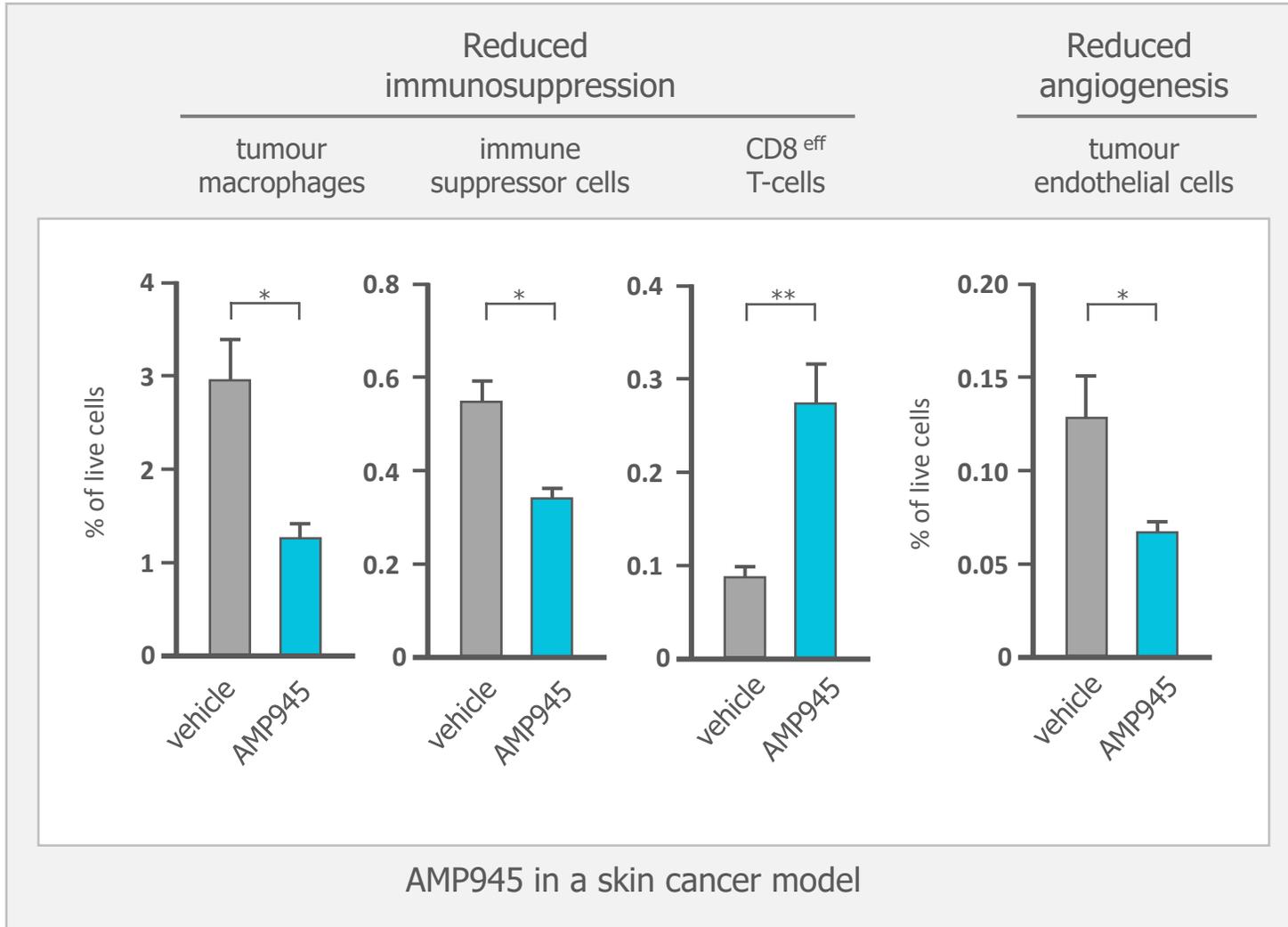
Focal Adhesion Kinase (FAK)

Fibrosis
FAK helps establish and maintain the dense, scar tissue around cancers
Immune activity
FAK triggers the release of signaling molecules (cytokines) which suppress the immune system
Cell migration
FAK regulates cell migration that is involved in the formation of secondary cancers (metastases)

- FAK is involved in many cancer defence mechanisms that reduce the effectiveness of cancer drugs
- Amplia is investigating the use of FAK inhibitors (FAKi's) to disrupt cancer defence mechanisms, making them more responsive to cancer drugs

**Remove the shield. Deliver the blow.**

# AMP945 – potential to enhance cancer treatments

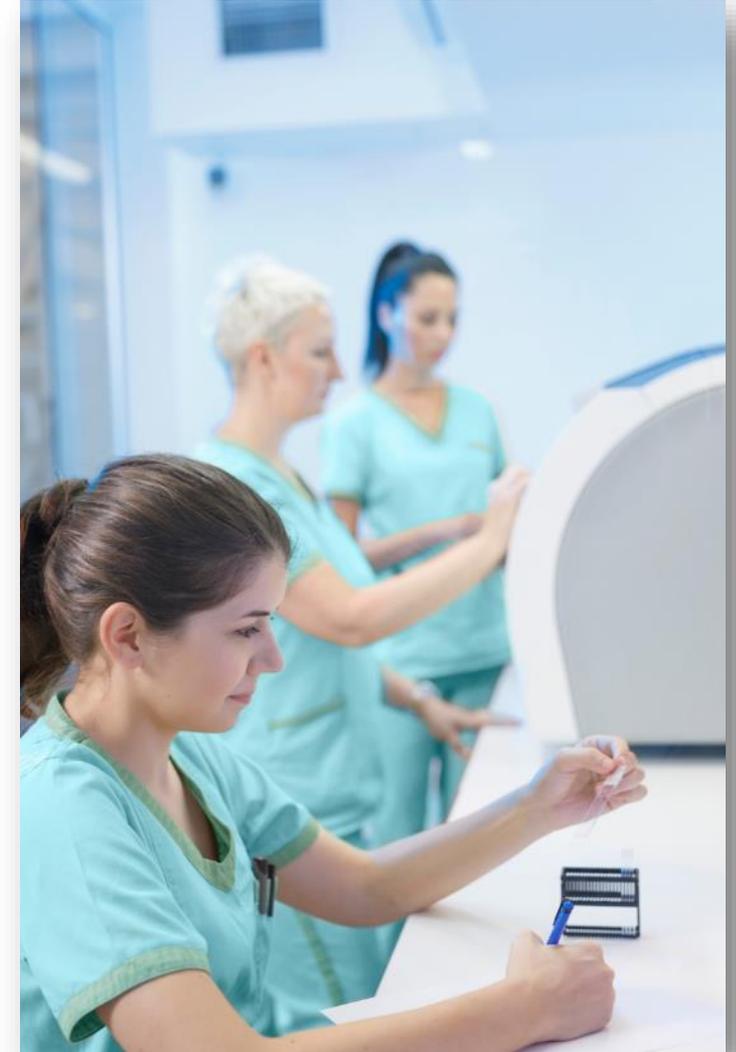


# AMP945 – treatment of solid tumours



## Pancreatic cancer

- Devastating disease with very poor outcomes
  - 5-year survival rate is 10.7%
  - Limited treatment options
- FDA Orphan Drug Designation for AMP945 in the treatment of pancreatic cancer received in March 2020
- Collaboration with Prof. Paul Timpson at the Garvan Institute
  - Combining FAK inhibitors with standard of care depletes pancreatic cancer defence mechanisms
  - Currently confirming effects with AMP945 before testing in clinic
  - Amplia plans to initiate pancreatic cancer trials in 2021



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# Fibrosis treatments



# FAK in lung fibrosis



Idiopathic Pulmonary Fibrosis (IPF) is a devastating, progressive disease caused by the build-up of fibrotic tissue in the lung which affects 3M people worldwide, including 130,000 in the US

Left untreated, the median survival time is 2-3 years, with lung transplantation the only treatment option currently available that improves outcomes

Approved drugs (pirfenidone and nintedanib) slow the progression of the disease by ~50%, but are unable to prevent the eventual loss of lung function:

- increase median life expectancy by 2½ years
- quality of life for end-stage disease remains very poor

**FAK has a pivotal role in the biochemical pathways regulating the development and progression of fibrosis in the lungs**



# Other opportunities in anti-fibrotic therapy



**Amplia is investigating a number of other fibrotic diseases could benefit from a FAK inhibitor**

## **Silicosis – non-clinical study commencing in Q1**

Silicosis is an industrial lung disease in which dust particles from sand, rock and minerals containing silica are inhaled and cause extensive scarring in the lungs making it hard to breathe

## **Non-alcoholic steatohepatitis (NASH) – non-clinical study underway**

Scarring of the liver caused by long-term inflammation and the build up of fatty tissues and is the most common chronic liver condition in Western populations (12% prevalence in the US)

## **Microbial respiratory infections**

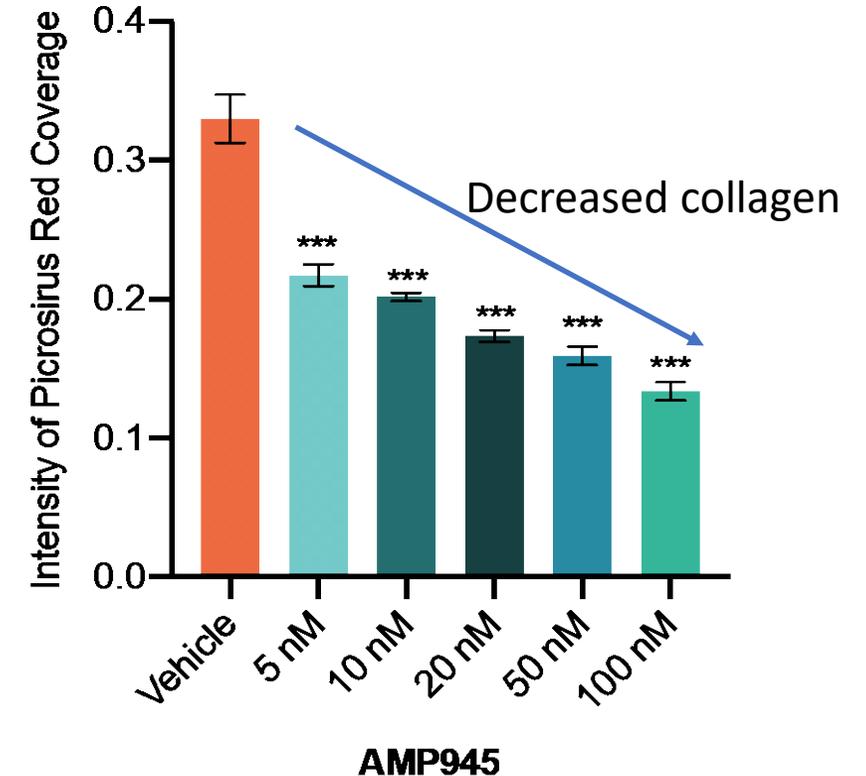
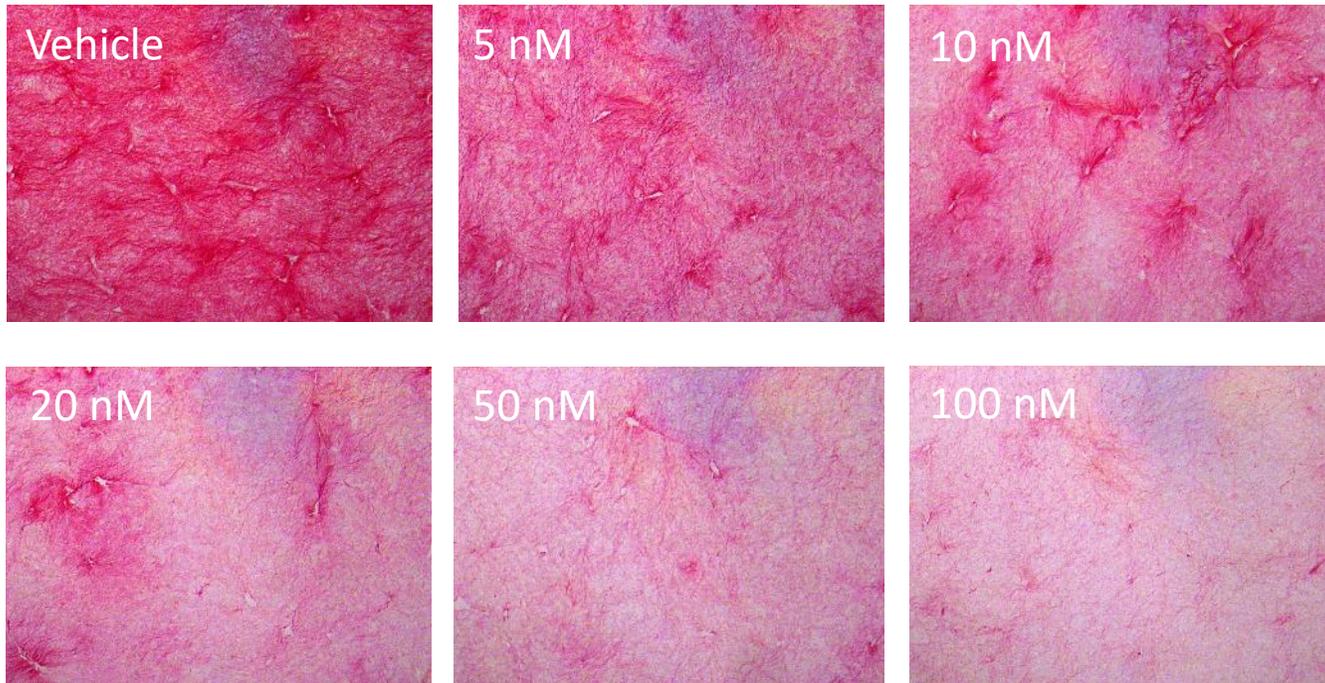
Many bacterial and viral infections damage lung tissue or induce an inflammatory responses that results in scarring and fibrosis which can have long term impacts on respiratory function



# AMP945 inhibits new collagen deposition *in vitro*



Picosirius red staining for total collagen

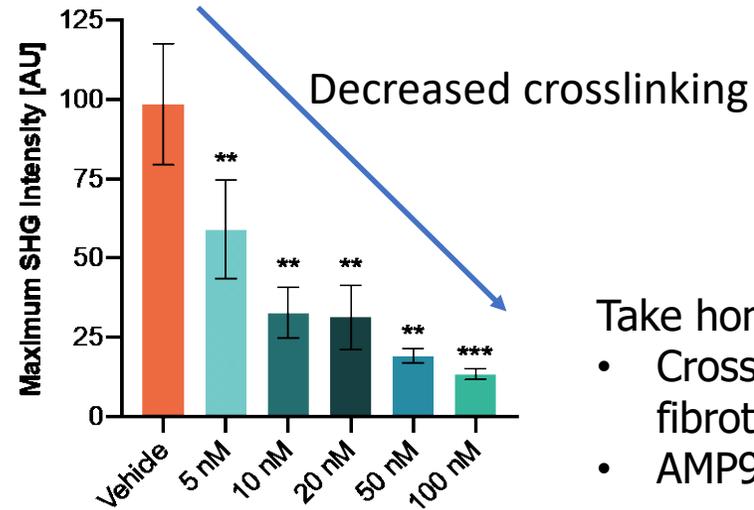
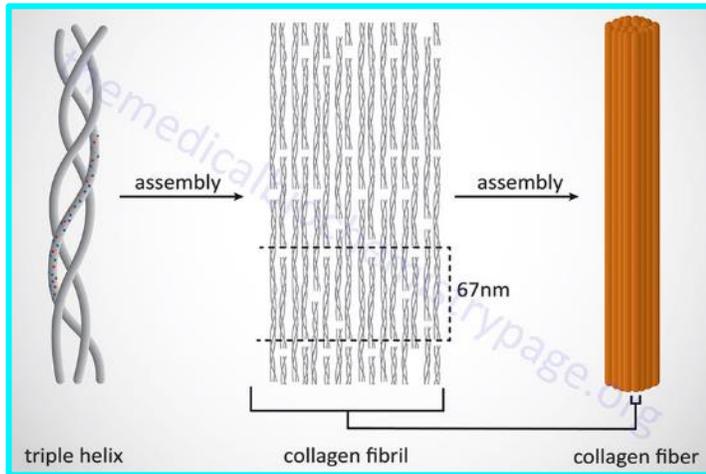


Take home messages:

- Collagen is one of the key building blocks of fibrotic tissue
- Fibroblasts remodel collagen and also lay down new collagen
- AMP945 inhibits fibroblasts, causing less new collagen to be deposited

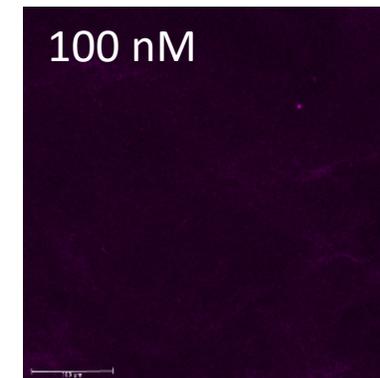
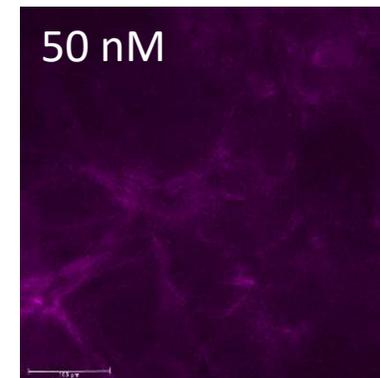
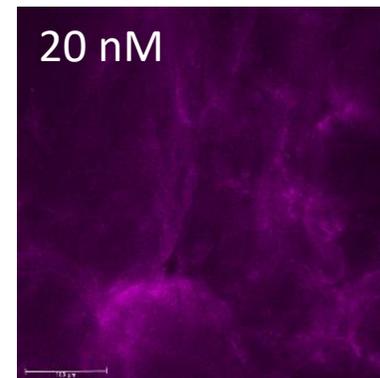
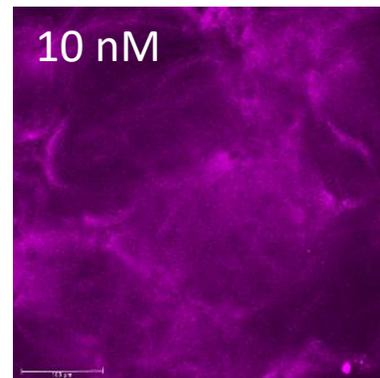
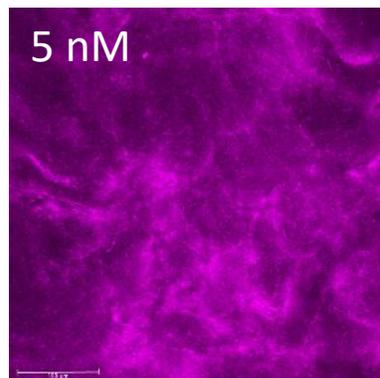
Data produced in the laboratory of Professor Paul Timpson (Garvan)

# AMP945 inhibits collagen cross-linking *in vitro*



Take home messages:

- Crosslinked collagen is a key building block of fibrotic tissues
- AMP945 inhibits collagen cross-linking

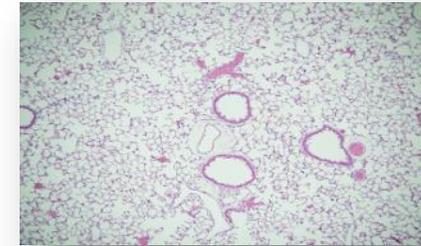


# AMP945 – prevention and treatment of lung fibrosis *in vivo*

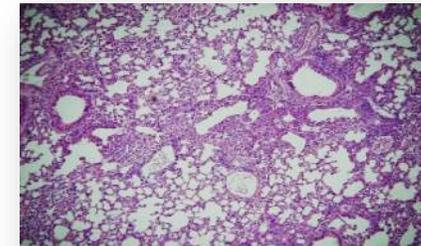


- Amplia holds FDA Orphan Drug Designation for AMP945 in the treatment of idiopathic pulmonary fibrosis (IPF)
- Preclinical studies of AMP945 using the industry-standard bleomycin model of lung fibrosis show that AMP945 is able to both:
  - Prevent onset of fibrosis
  - Treat established fibrosis

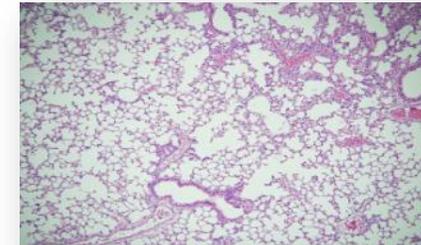
**control – healthy lung**



**bleomycin – fibrotic lung**



**bleomycin + AMP945**



# Program Status and Plans

# Amplia's Lead Drug Candidate – AMP945



- Parallel development underway in both pancreatic cancer and fibrosis
  - Orphan Drug Designations received from FDA for AMP945 in both pancreatic cancer and idiopathic pulmonary fibrosis
  - Kilo-scale manufacture undertaken
  - Phase 1-enabling toxicology studies completed June 2020
  - Phase 1 trial initiated October 2020
    - Healthy volunteer trial design supports Phase 2 in both cancer and fibrosis patients
    - Concurrently, Amplia is preparing for Phase 2 clinical trials in both cancer and fibrosis



# First human trial of AMP945 is underway



- In October 2020, Amplia commenced dosing subjects in the first clinical trial of AMP945
- Phase 1 clinical trial in healthy volunteers:
  - Approximately 64 healthy volunteers
  - Single ascending dose, multiple ascending dose
  - Safety, pharmacokinetic and exploratory pharmacodynamic studies
- Trial expected to complete in Q2, with top-line data available in mid-2021
- Data from Phase 1 trial expected to support progression of AMP945 into more advanced clinical testing in patients with cancer and fibrotic diseases



# Phase 1 Trial Update



- Single ascending doses tested so-far
  - Well tolerated
  - No safety concerns so-far
  - Showing excellent pharmaceutical properties
- Multiple ascending dose expected to start soon
- On track to complete dosing in Q2 2021



# Phase 2 Planning - Pulmonary Fibrosis

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- Amplia proposes to accelerate its clinical development plans in pulmonary fibrosis
  - Phase 1 trial on track
  - Recent discussions with pulmonary clinicians indicate significant interest in running a Phase 2 trial in pulmonary fibrosis patients
  - New preclinical evidence arising from Timpson laboratory builds on bleomycin lung fibrosis model data previously in hand
- Status
  - Clinician engagement in trial protocol is ongoing
  - Planned enabling activities
    - Phase 1 results (funded)
    - Extended (3 month) toxicology studies
    - Manufacture of AMP945 to supply toxicology studies and Phase 2 trial
    - Trial setup

# Provisional Pulmonary Fibrosis Trial Design



- Key design elements
  - Patients with known progressive interstitial lung disease
  - Up to 3 months' dosing with AMP945
  - Compare safety and efficacy of AMP945 to placebo
    - 2-3 dose levels expected, ~10 patients per group
  - 4x Australian sites
    - Potential to expand to US sites under IND
  - Key outcome measures
    - Functional imaging
    - Spirometry
    - Biomarkers
    - Cough questionnaire



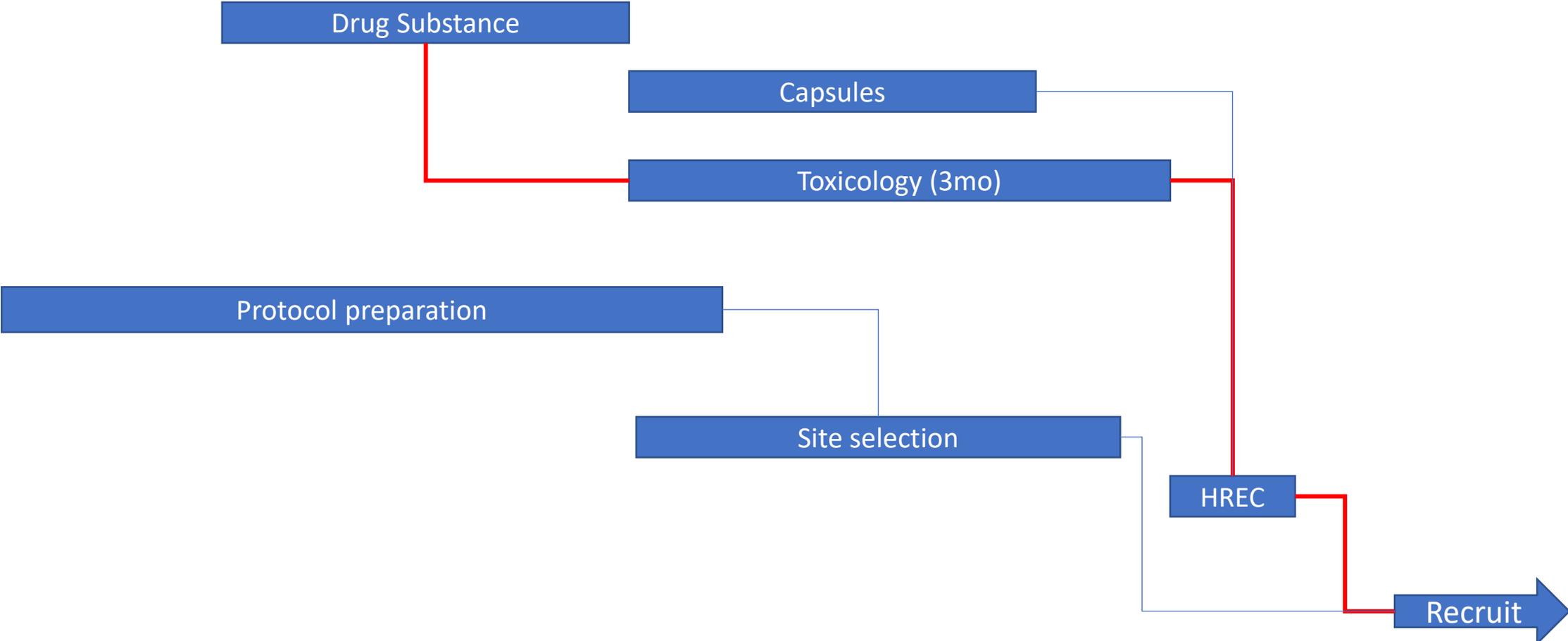
# Projected Timeline



**2021**

**2022**

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr



# Phase 2 Planning – Pancreatic Cancer

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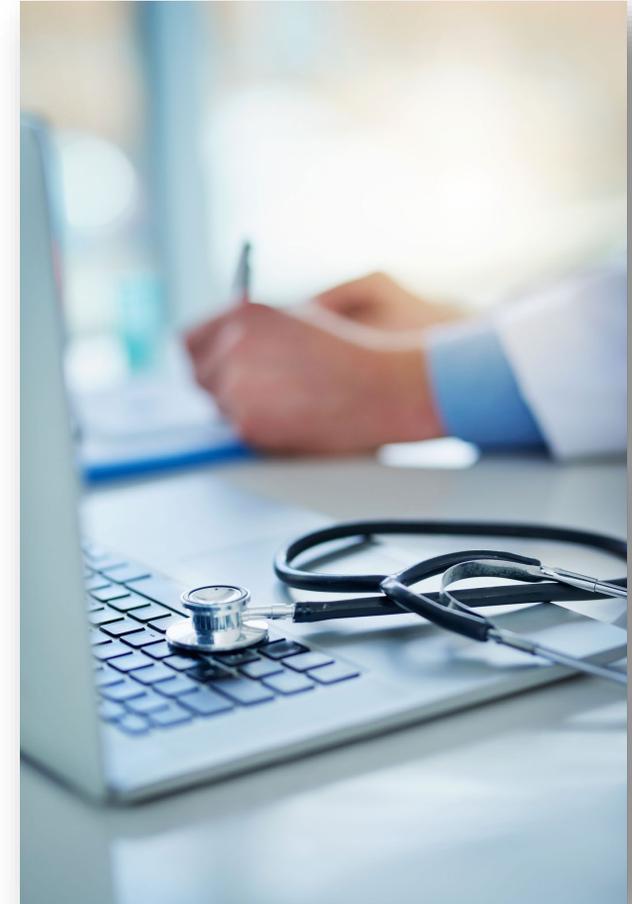


- Trial design expected to be combination study of AMP945 with a standard of care
- Final design is subject to preclinical data currently being generated
- Subject to results, pancreatic cancer trial may start earlier than pulmonary fibrosis trial
- Status
  - Clinician engagement in early stages
  - Planned enabling activities
    - Phase 1 results (funded)
    - Manufacture of AMP945 to supply Phase 2 trial
    - Trial setup

# Provisional Pancreatic Cancer Trial Design



- Selected design elements
  - Patients with unresectable pancreatic cancer
  - Combination therapy of AMP945 and gemcitabine/abraxane in novel dosing regimen
  - Compare safety and efficacy of combination therapy to standard of care alone
    - 60-80 patients
    - Australian sites
    - Potential to expand to US sites under IND
- Outcome measures
  - Overall survival
  - Progression free survival
  - Objective response (RECIST)
  - Safety





[ampliatx.com](https://ampliatx.com)