ABN 16 165 160 841

ASX RELEASE **23 February, 2023**

US CONFERENCE PRESENTATION

- *Amplia's FAK inhibitor program to be presented at Next Generation Kinase Inhibitors Summit in Boston, USA*

Melbourne, Australia: Amplia Therapeutics Limited (ASX: ATX), ("Amplia" or the "Company"), a company developing new approaches for the treatment of cancer and fibrosis, is pleased to announce that Amplia Head of Translational Biology, Dr Terrie-Anne Cock, will present a lecture at the **2nd Next Generation Kinase Inhibitors Summit** currently underway in Boston, USA.

The presentation, entitled '*Targeting Focal Adhesion Kinase (FAK) for the treatment of cancer and fibrotic diseases*' describes preclinical and Phase 1 clinical data for Amplia's lead FAK inhibitor AMP945. A copy of the presentation, to be given at Friday 6:30am AEDT, is attached to this announcement.

Amplia CEO, Dr Chris Burns, commented: "Being invited to present our research at such a highly respected, industry-focused conference devoted to kinase inhibitor drug development, reflects the importance of our research at Amplia and our standing in the kinase field, internationally. Further, it allows us to promote the quality of the work being conducted at Amplia to biotech and pharma companies around the world."

This ASX announcement was approved and authorised for release by the CEO of Amplia Therapeutics.

- End -

Investor Contact:
Dr Chris Burns
Chief Executive Officer
chris@ampliatx.com

Media Contact:
H^CK Director, Haley Chartres
haley@hck.digital
+61 423 139 163

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 fibrotic cancers such as pancreatic cancer. FAK also plays a significant role in several chronic diseases, such as idiopathic pulmonary fibrosis (IPF). For more information visit www.ampliatx.com and follow Amplia on Twitter (@ampliatx) and LinkedIn.

Targeting Focal Adhesion Kinase (FAK) for the treatment of cancer and fibrotic diseases

Terrie-Anne Cock PhD

Amplia Therapeutics, Melbourne, Australia

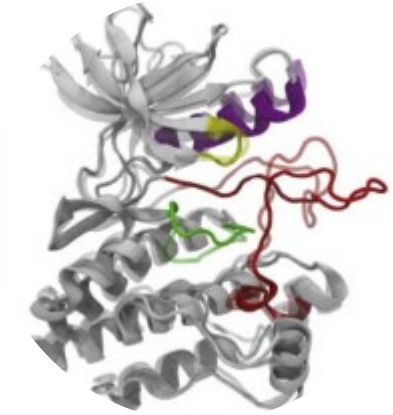
Amplia Therapeutics Limited

Amplia
Exposing cancer. Enhancing treatment.

Focal Adhesion Kinase

Fibrotic Tissue

Promotes fibrosis



Focal Adhesion Kinase (FAK)

Shields tumours from chemotherapy

Fibrotic tumourmicroenvironment

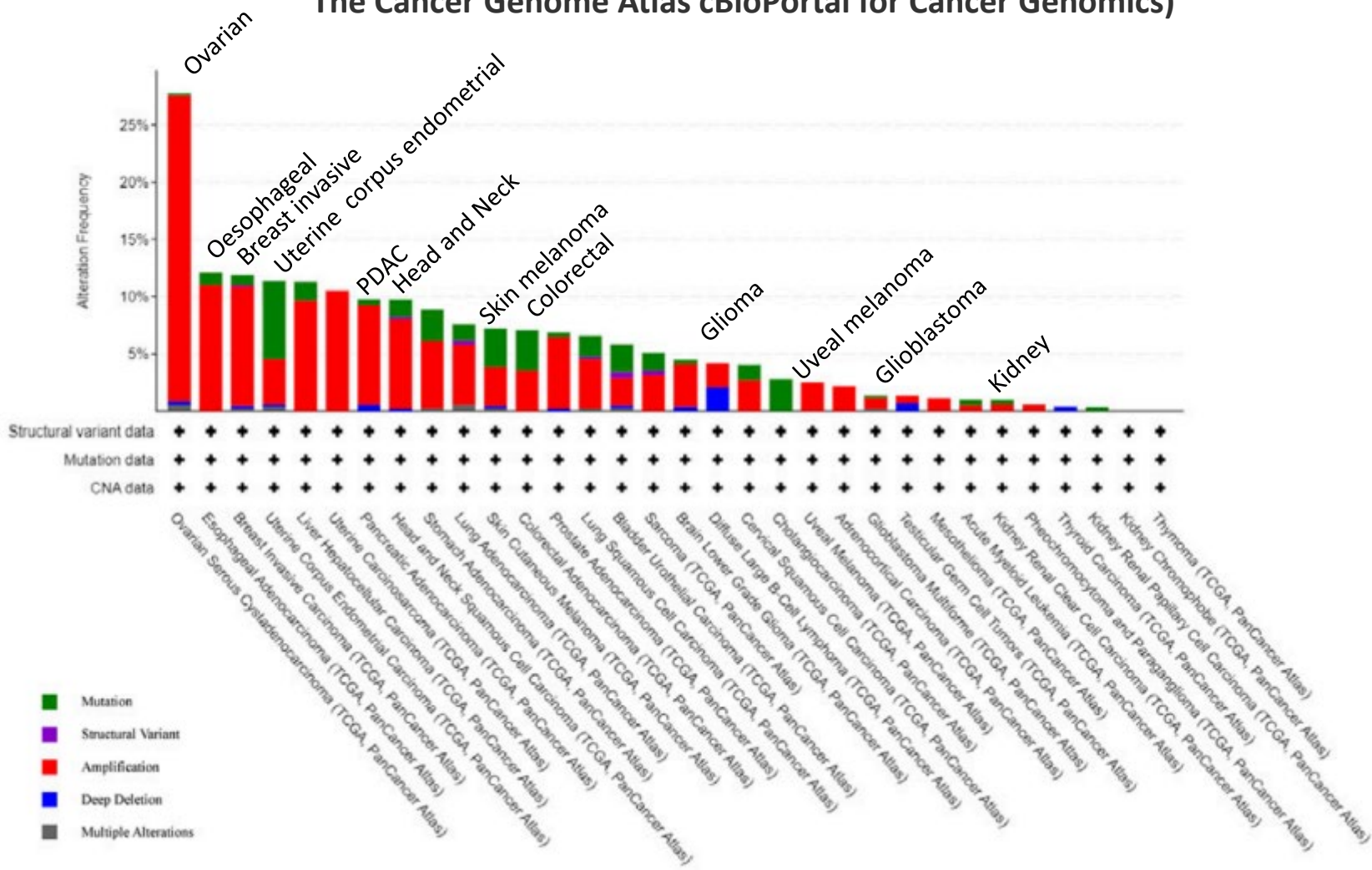
Fibrotic Diseases

Solid Cancers

FAK association with cancer

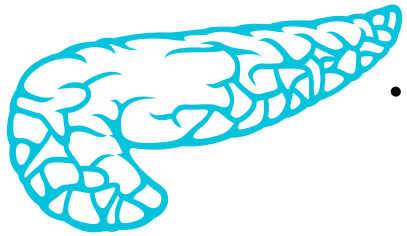
- **FAK is rarely mutated in cancer**, most frequently occurring in cancers arising from the uterus (9.24% of samples), colon (7.25%) and liver (3.92%) with simple somatic mutations resulting in a missense, stop or frameshift
- **FAK expression is very commonly increased or 'gene-amplified' in a number of cancers**
- **In many cancers FAK increase is predictive of poor patient outcome**

Percentage of tumour samples with increased FAK mRNA: The Cancer Genome Atlas cBioPortal for Cancer Genomics)



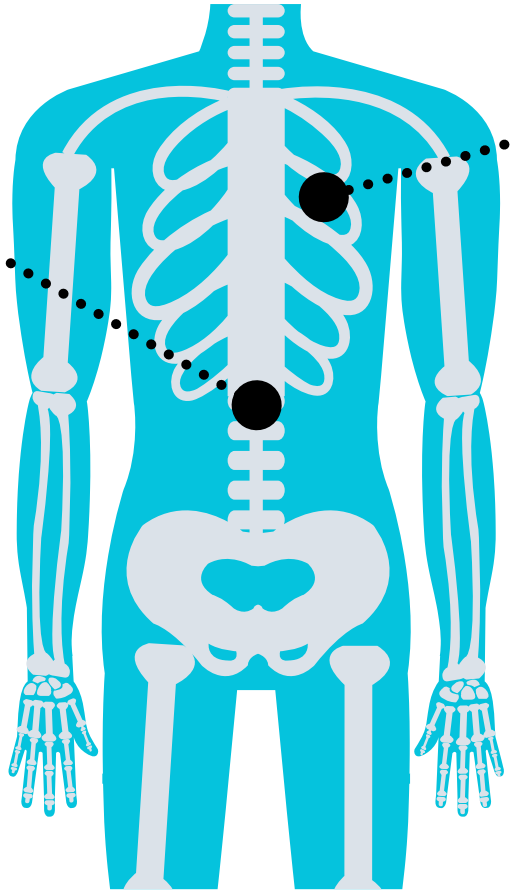
Front Cell Dev Biol. 2022 Nov 2;10:1040311.

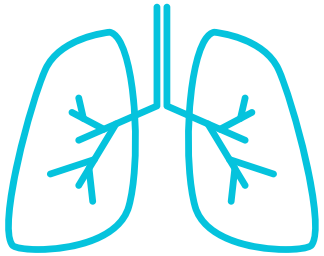
Amplia's Focus



Pancreatic Cancer

- 60,000 new diagnoses and 48,000 deaths from pancreatic cancer in the US each year*
- Difficult-to-treat cancer
- Less than 20% of patients eligible for surgery
- Most patients treated with cytotoxic chemotherapy drugs





Idiopathic Pulmonary Fibrosis (IPF)

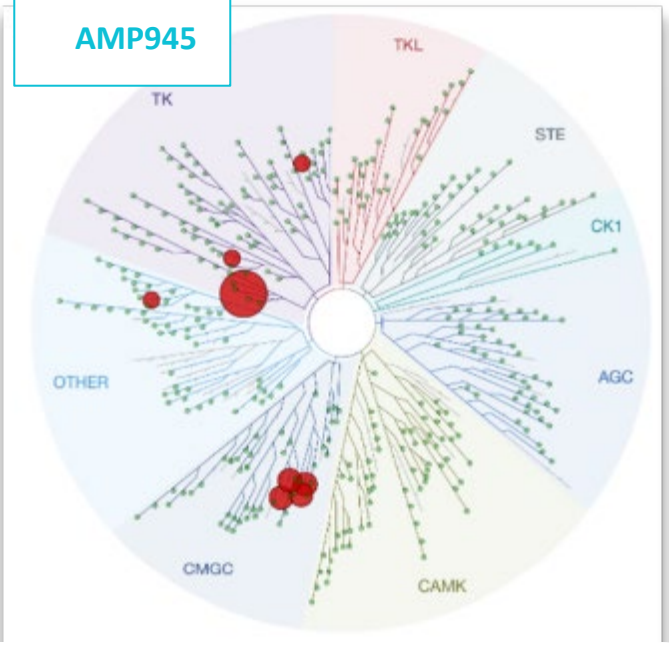
- Affects ~3M people worldwide**
- Devastating, progressive disease caused by the build up of fibrotic tissue in the lungs
- Two drugs approved which only slow progression
- Median survival time is 3-5 years

* American Cancer Society, 2021

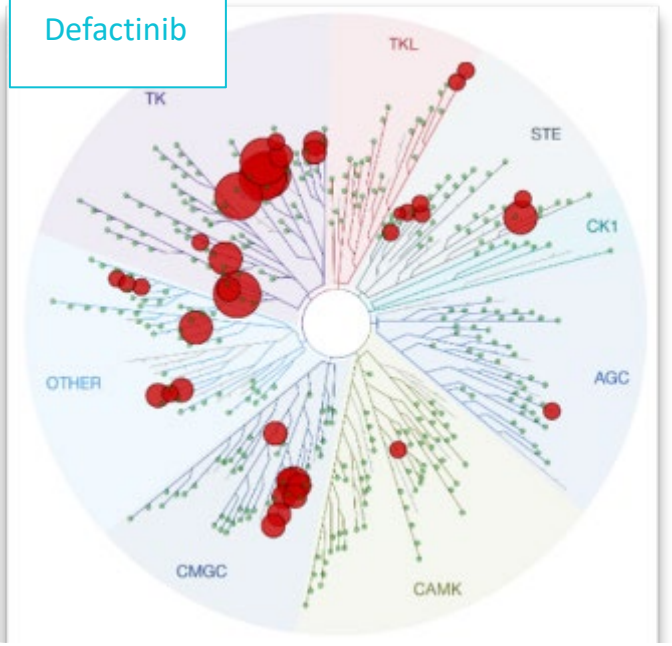
**The American Journal of Managed Care, 2021

AMP945 is a potent and selective FAK inhibitor

AMP945



Defactinib

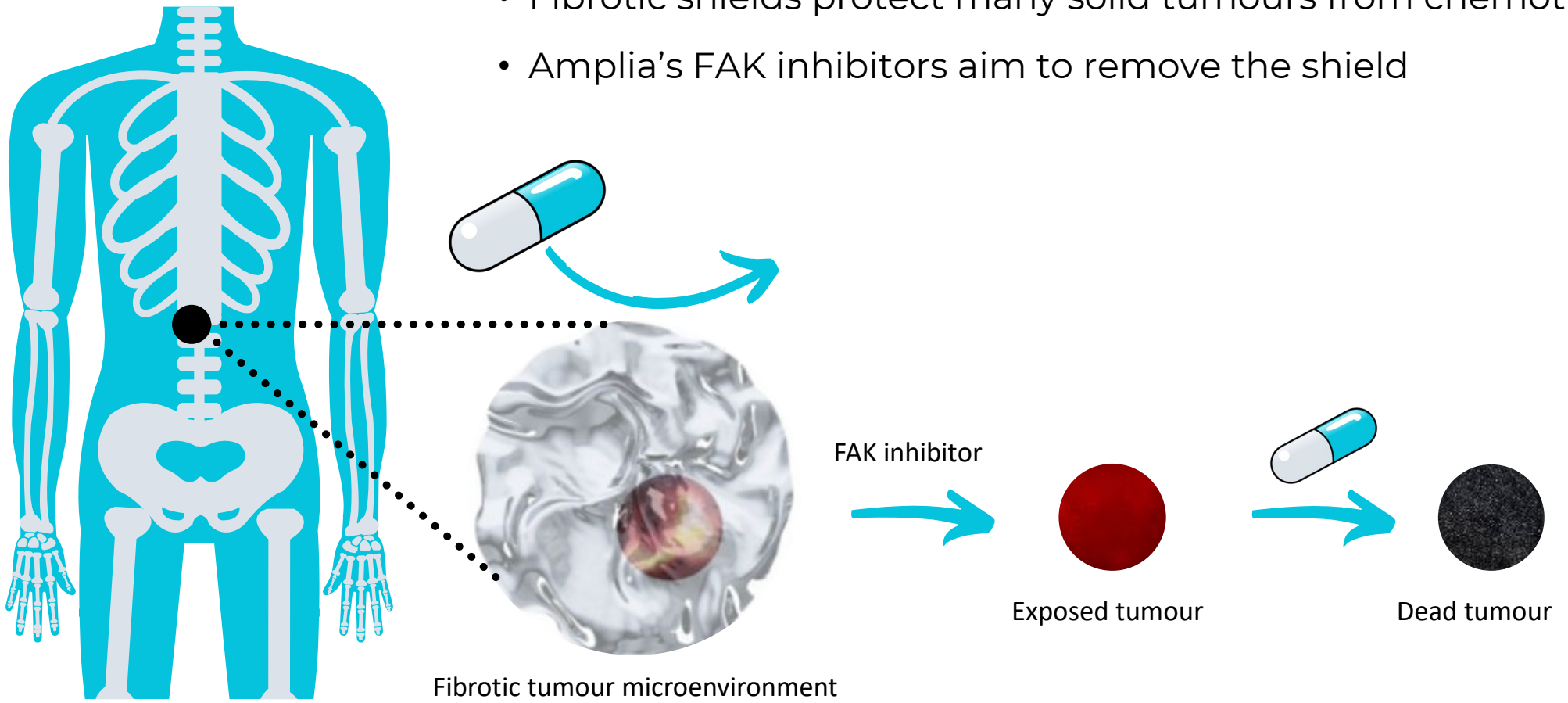


AMP945 is the most selective FAK inhibitor in clinical development

FAKi	**AMP945**	Defactinib	IN10018
Company	**Amplia**	Verastem	InxMed
IC50 >1 µM	**3 (468 kinase tested)**	9 (468 kinase tested)	4 (262 kinase tested)

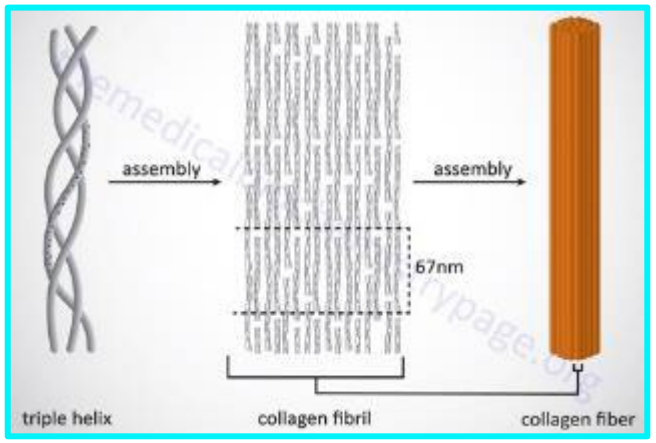
Amplia's Hypothesis | Enhancing Chemotherapy

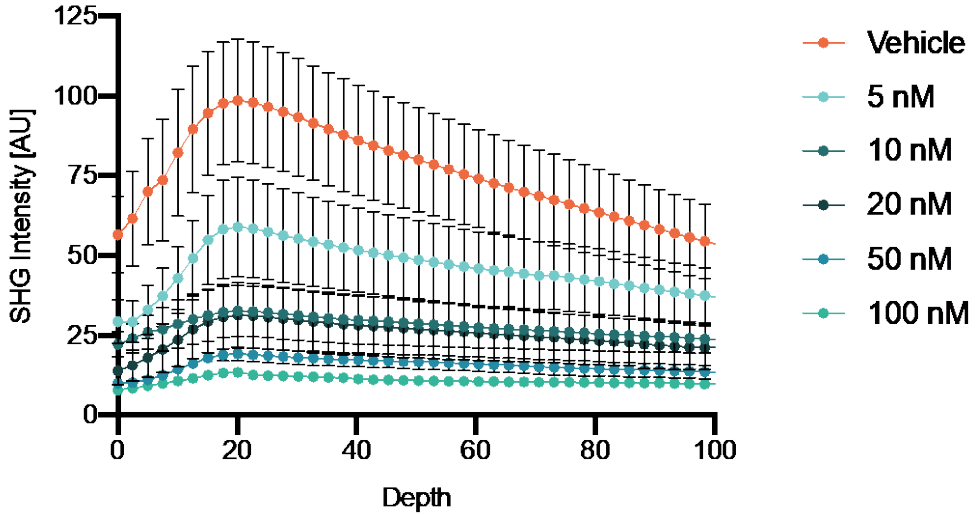
- Fibrotic shields protect many solid tumours from chemotherapy
- Amplia’s FAK inhibitors aim to remove the shield

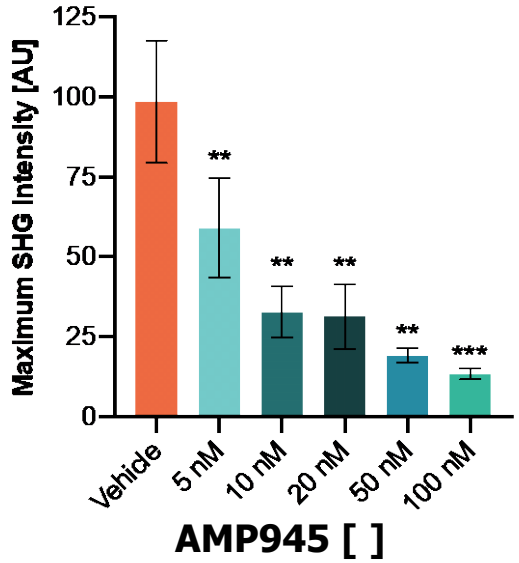


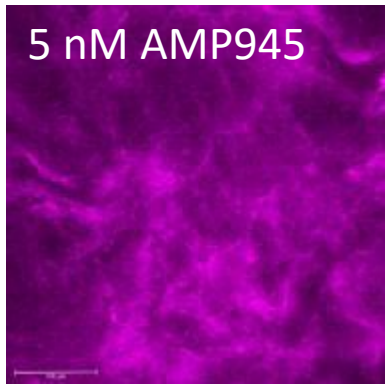
AMP945 inhibits collagen cross-linking *in vitro*

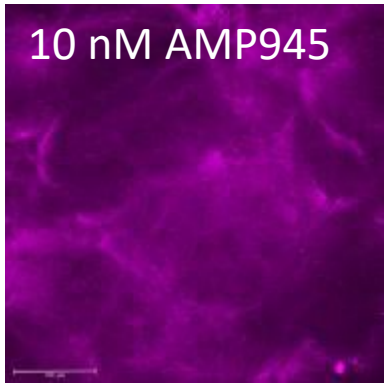
Second Harmonic Generation measures only cross-linked collagen

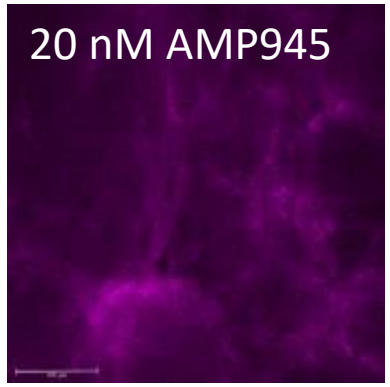


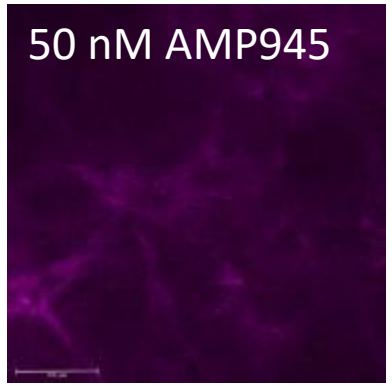


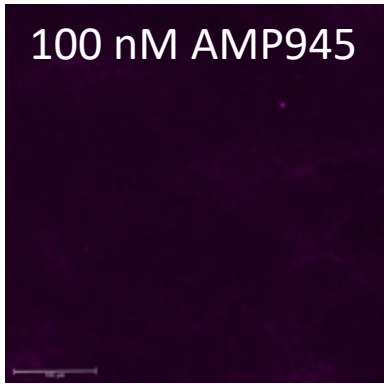








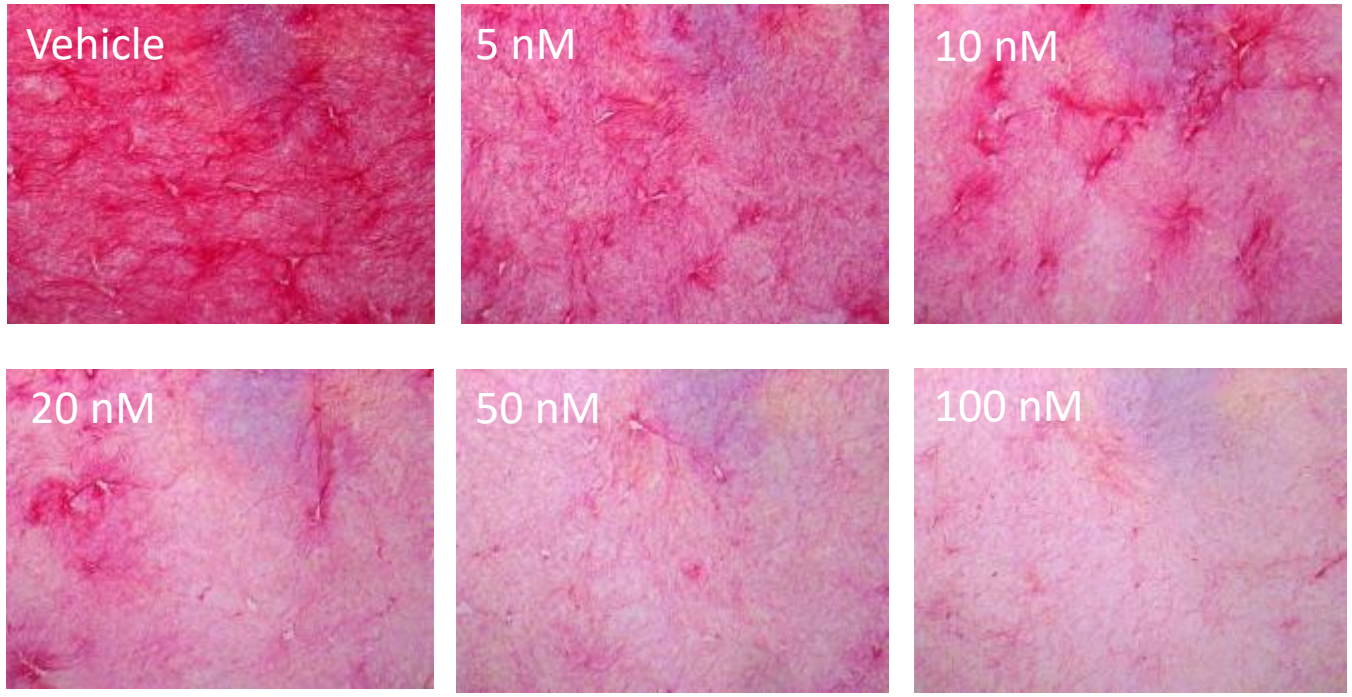


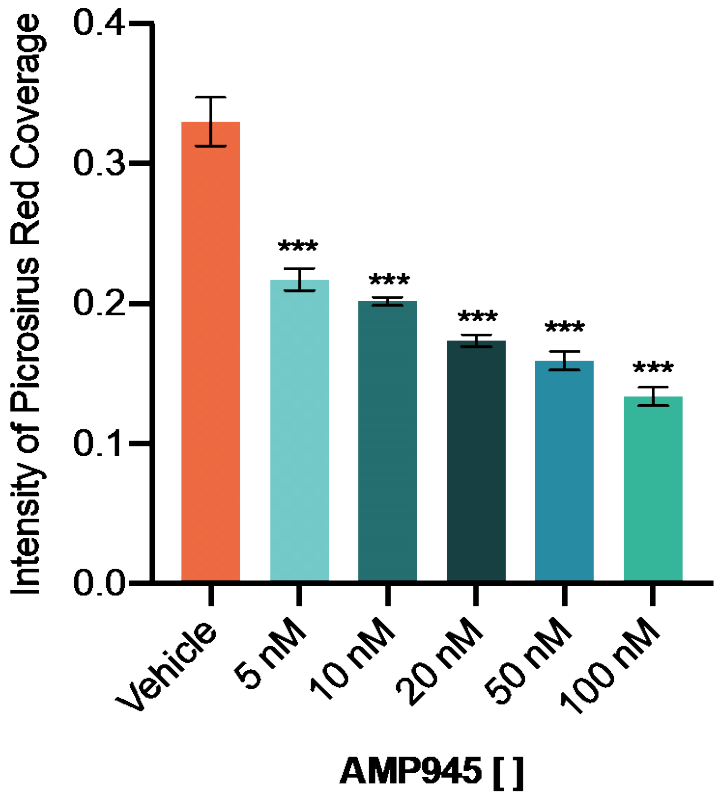


Timpson Lab (Garvan Inst.)

AMP945 inhibits new collagen deposition *in vitro*

Picosirius red staining for total collagen





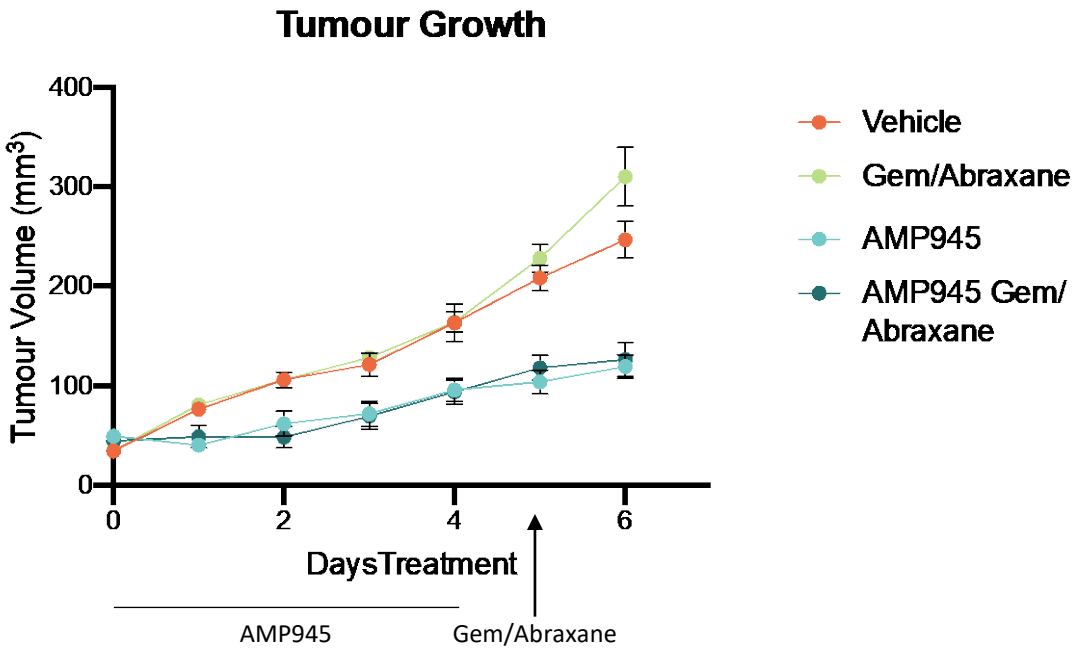
Take home messages:

- Fibroblasts remodel collagen and also lay down new collagen
- AMP945 causes less new collagen to be deposited by the fibroblasts

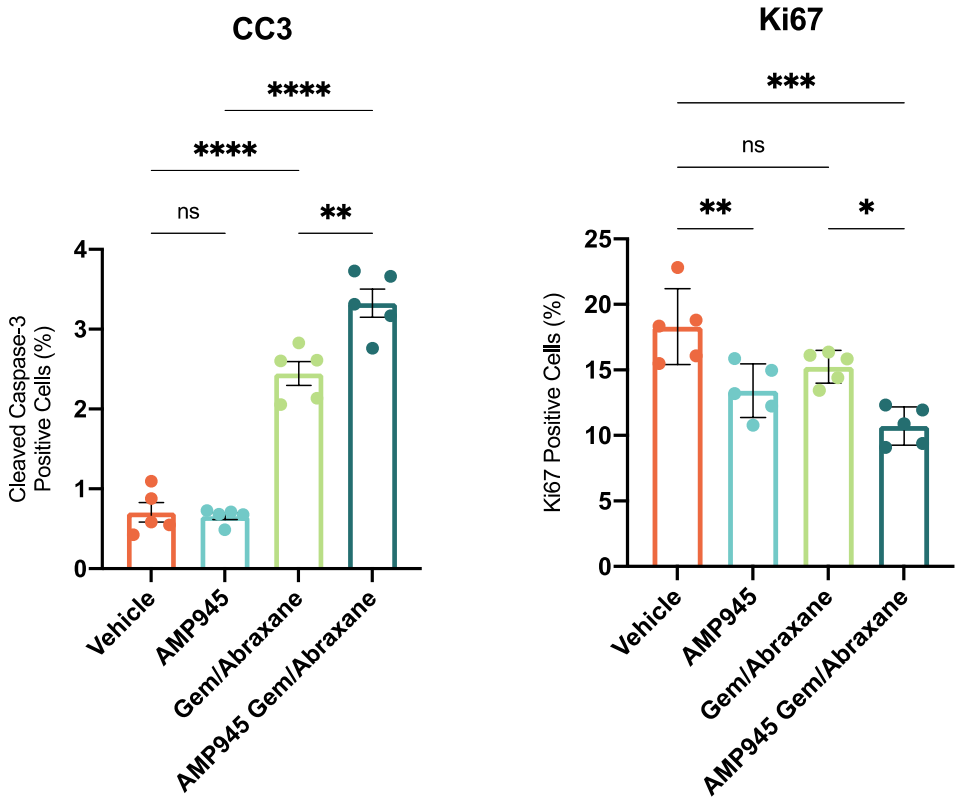
Timpson Lab (Garvan Inst.)

AMP945 'priming' enhances cleaved caspase 3 and Ki67 response to standard of care Gemcitabine + Abraxane treatment (Day 6)

KPC mouse model is a clinically relevant model of pancreatic ductal adenocarcinoma

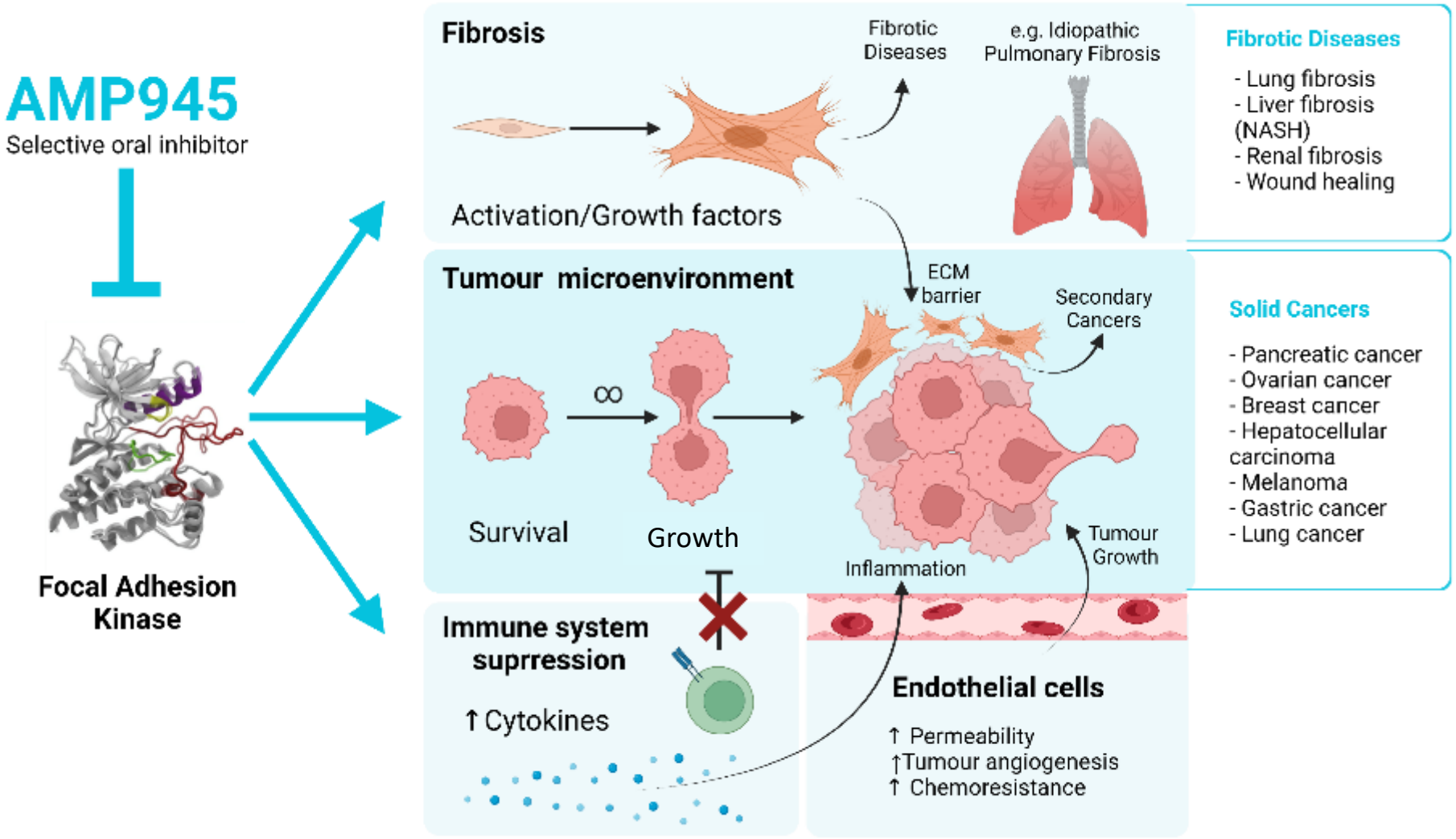


Tumors analysed 24 hrs post Gem/Abraxane administration



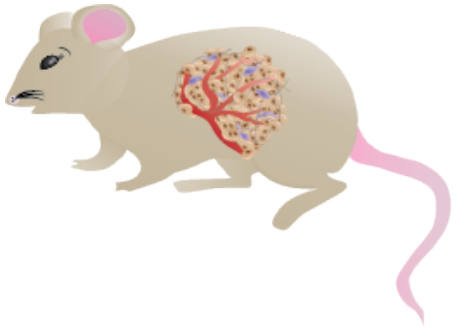
Timpson Lab (Garvan Inst.)

FAK – a drug target for multiple cancers and fibrotic diseases



Murphy, J. M., et al. (2020). *Experimental & molecular medicine*, *52*(6), 877–886.
Wu, Y., et al. (2021). *Discover. Oncology*, *12*(1), 52.

Priming with FAKi AMP945 in the subcutaneous KPC mouse model of pancreatic cancer



Subcutaneous Injection $1x10^6$ Cells

Repeated treatment cycle

FAKi Priming
10 mg/kg Oral Administation

am am am
pm pm pm
Day 1 Day 2 Day 3 Day 4

IP Injection gem/Abraxane
Day 7

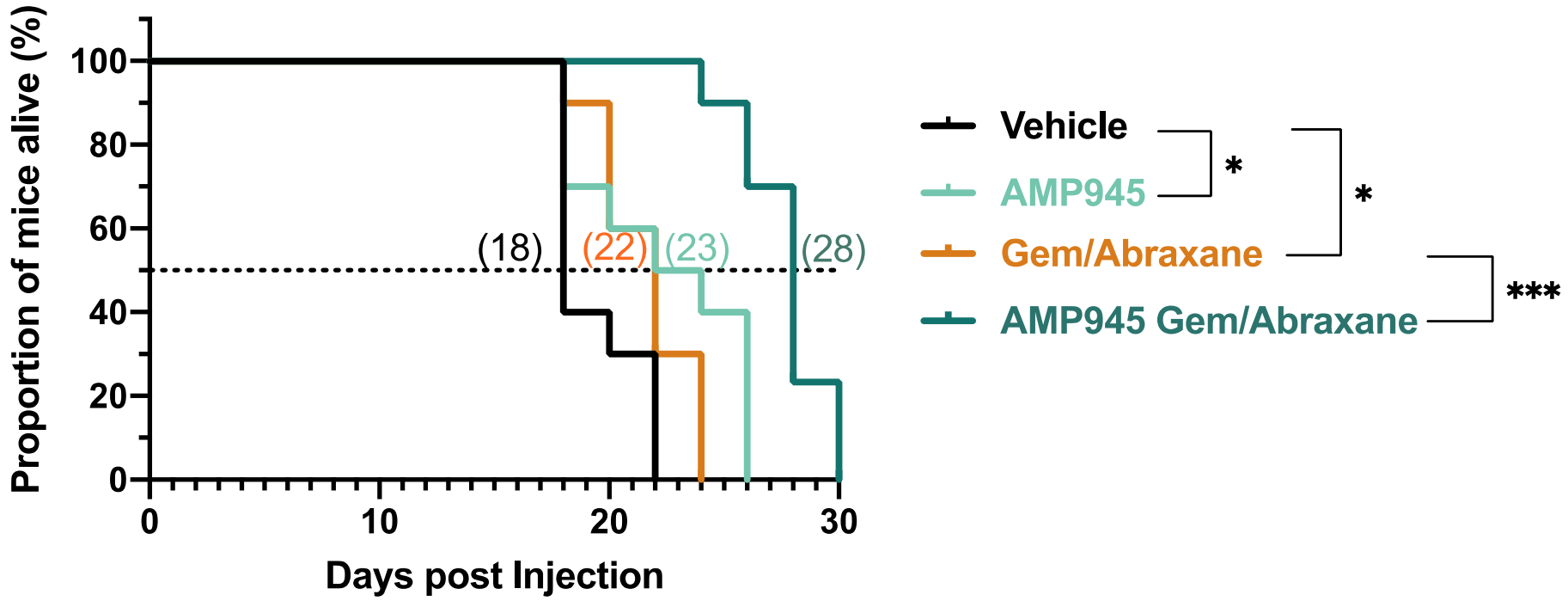
IP Injection gem/Abraxane
Day 10

Day 12

Time line
Tumour Establishment
Palpable Tumour

AMP945 enhances survival to gemcitabine and Abraxane in an aggressive mouse model of pancreatic cancer

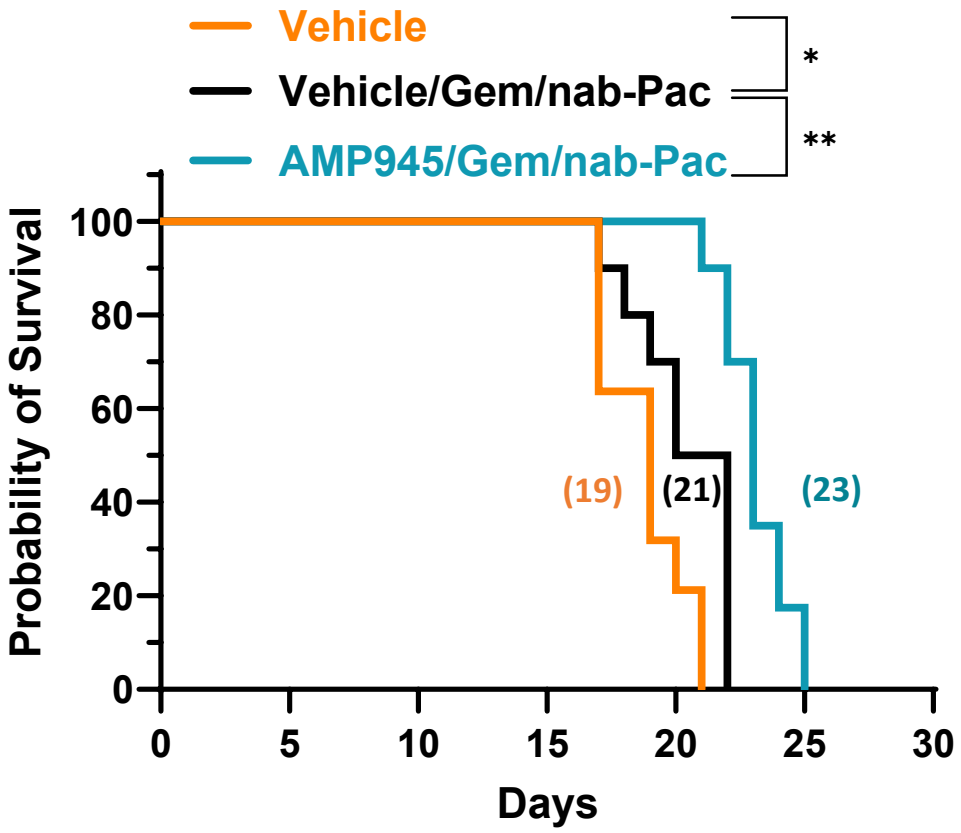
Survival in the KPC mouse model of pancreatic cancer



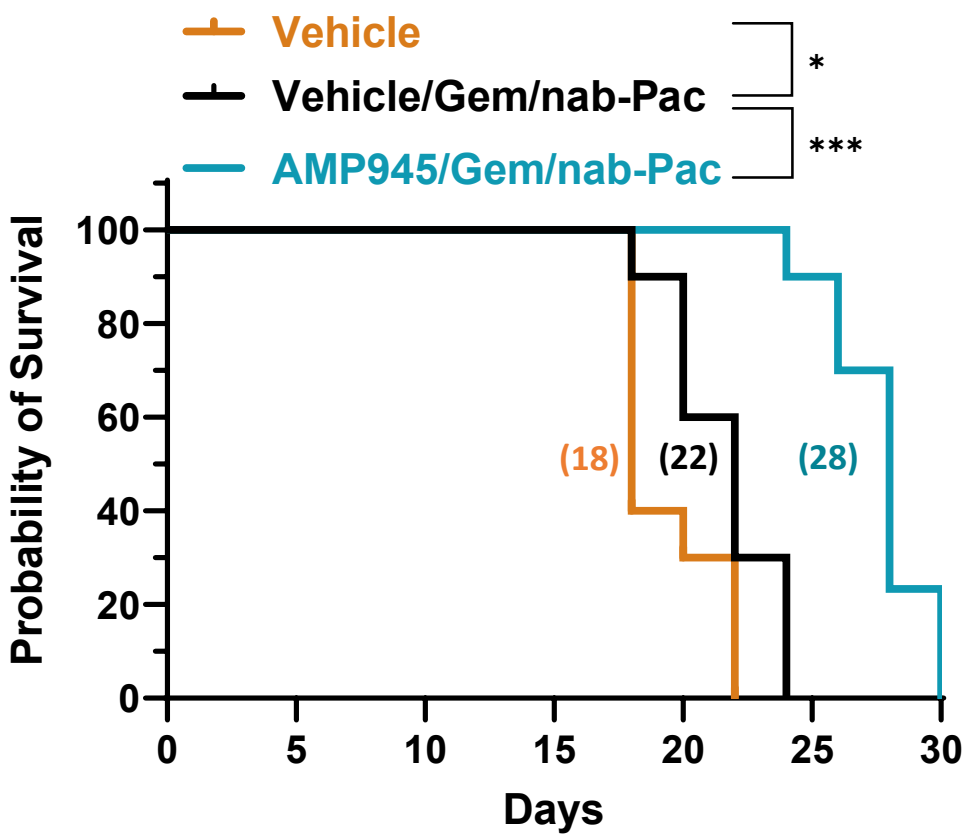
* P ≤ 0.05
*** p ≤ 0.005

Priming is more effective than continuous daily dosing

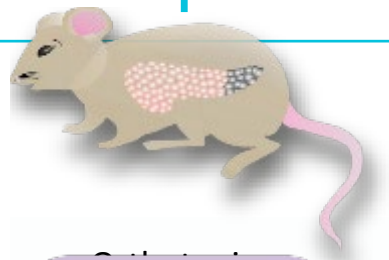
Daily dosing AMP945 for each cycle



Priming for first 4 days of each cycle



AMP945 Improves Survival in PDX Pancreatic Cancer Model



Orthotopic Injection (in pancreas)

Treatment with AMP945 or vehicle, twice daily, AM and PM

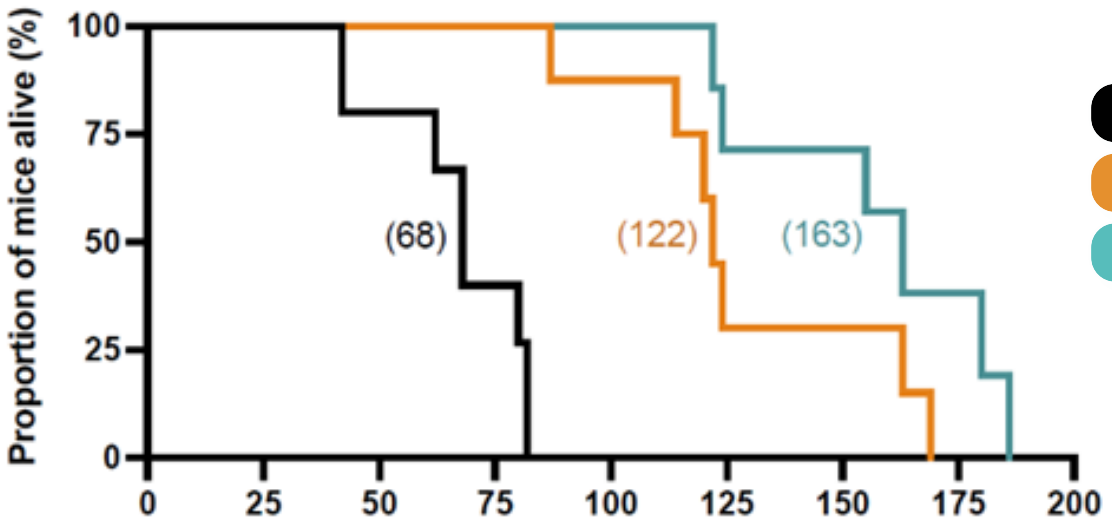
Treatment with Gemcitabine/Abraxane or vehicle

Day 1 PM AM PM AM PM AM **Day 7** **Day 10**

≥ 7 days of acclimatization

Tumour growth until palpable

Repeat up to **20 cycles** or until experimental endpoint reached



TKCC-10-LO Orthotopic Model

- Vehicle
- gemcitabine / nab-paclitaxel
- AMP945 / gemcitabine / nab-paclitaxel

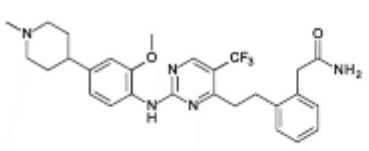
P ≤ 0.0001

P ≤ 0.05

A phase 1 trial of AMP945, a potent and selective focal adhesion kinase inhibitor, in healthy volunteers

Randomized, double-blinded, placebo-controlled in healthy volunteers (18 - 50 years)

AMP945



Single ascending dose (SAD)

Placebo

AMP945 *Fasted*

AMP945 *Fed*

n=2

n=2

n=2

n=2

15mg n=6

30mg n=6

60mg n=6

125mg n=6

Wash out period

Multiple ascending dose (MAD)

Placebo

AMP945

7 Consecutive days

n=2

n=2

n=2

25mg n=6

50mg n=6

100mg n=6

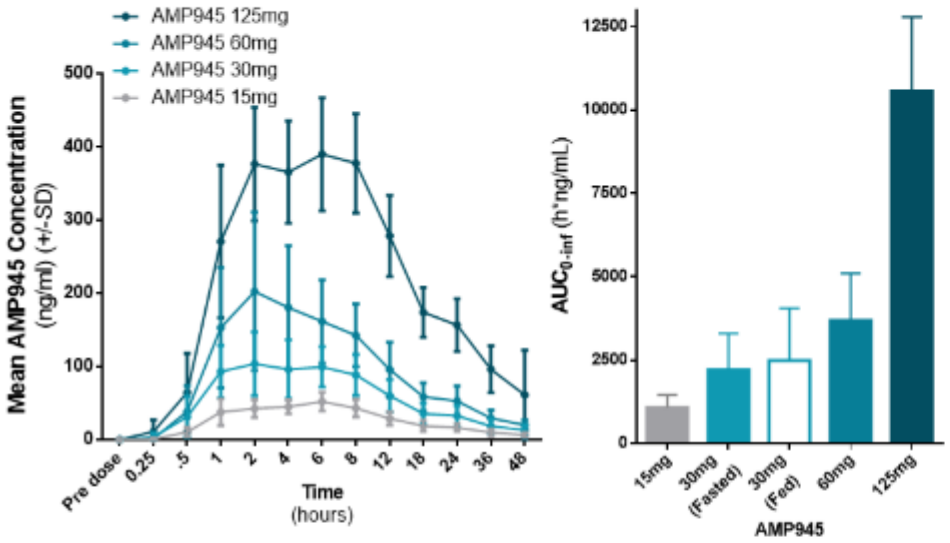
Outcomes

	Single ascending dose (SAD)	Multiple ascending dose (MAD)
Blood Collection Pharmacokinetic analyses	Pre-dose and 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24, 36, and 48 h post-dose	Pre-dose and 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24, 36, and 48 h post-dose and up to 24 h post-dose on Days 1 and 7
Skin Biopsy Pharmacodynamic analyses	Before and after dosing with 125 mg	Before and after dosing with 25, 50, 100mg

Safety and tolerability were assessed according to incidence and severity of adverse events (AEs).

Results – plasma pharmacokinetics of AMP945

Single ascending dose (SAD)



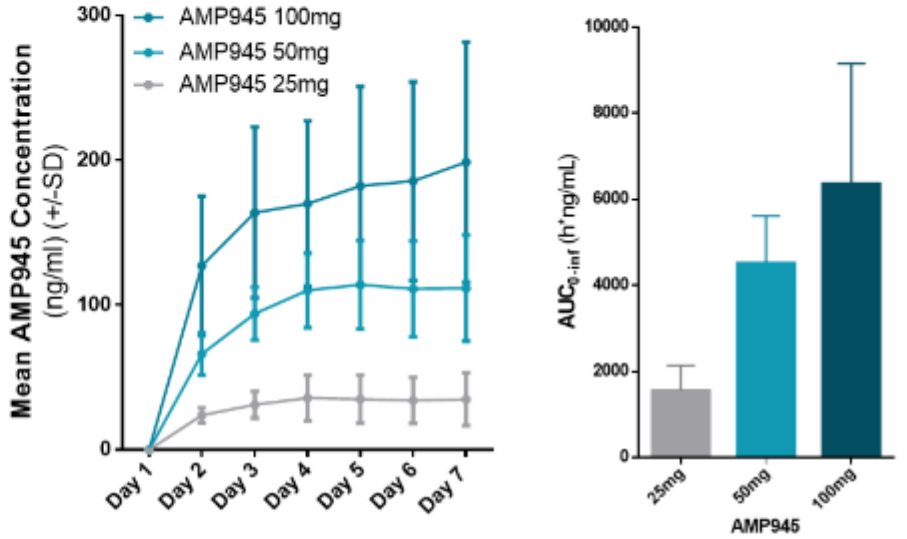
- Food consumption did not result in a change of AMP945 pharmacokinetics.
- **Mean time to maximum plasma concentration:** 1 to 6 h
- **Median half-life** ranged from 15.7 to 23 h

→ Supports feasibility of QD dosing

- **Mean apparent volume of distribution** ranged from 328 to 463 L

→ Indicates Tissue wide distribution

Multiple ascending dose (MAD)

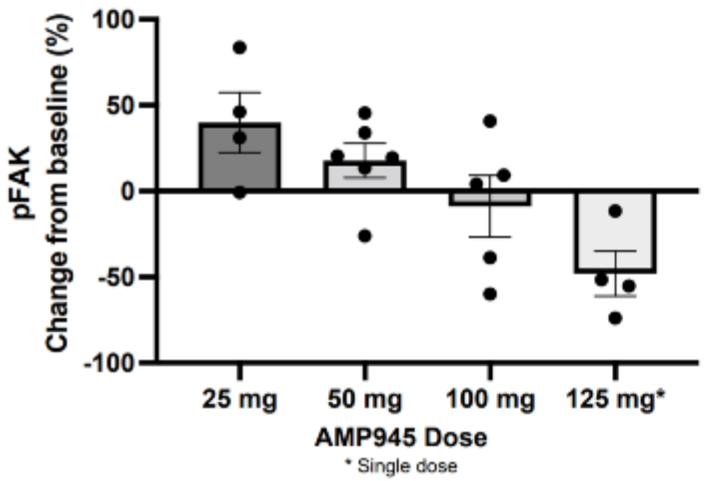


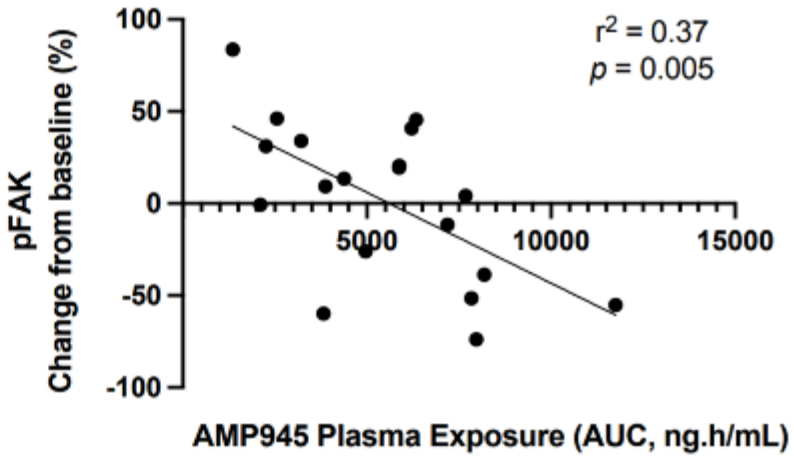
- **Mean time to maximum plasma concentration:** 2 to 4 h

- Observations of pre-dose trough levels between Day 1 and Day 7 indicated that steady state was achieved by Day 4 to Day 5 (approximately 5 x t1/2)

Results – Pharmacodynamics and safety

Dose- and Exposure-response analysis for phospho-FAK (pFAK) levels in skin punch biopsies from healthy volunteers





- **Significant (linear) relationship** observed between the change in FAK activity from baseline and AMP945 $AUC_{0\text{-}inf}$ following dosing with 25, 50, 100 and 125 mg of AMP945.

Safety Summary

- No serious or severe TEAEs, nor any TEAEs leading to study withdrawal (majority of TEAEs reported were mild)
- There were no dose-related trends observed in the reporting of TEAEs
- No TEAEs were considered probably or definitely related to AMP945
- No changes over time or dose-related trends in clinical safety laboratory parameters;
- No changes over time or dose-related trends in vital signs, ECG, physical examination and concomitant medications reporting

Conclusions - Phase 1 trial of AMP945

- AMP945, a selective FAK inhibitor, **was safe and well tolerated** across SAD (15 to 125 mg) and MAD (25 to 100 mg) cohorts in healthy volunteers
  - No serious adverse events or withdrawals
  - No trends observed in AE reporting, no shifts in clinical laboratory, vital signs, ECGs
- AMP945 PK and PD data demonstrate **wide tissue distribution and target engagement**
  - Predictable dose/exposure relationship
  - Achieved blood levels of AMP945 expected to inhibit FAK
- Supports continued development of AMP945 in patients with solid tumours and fibrotic diseases in which FAK inhibition would be beneficial

Phase 2 pancreatic cancer clinical trial "ACCENT"

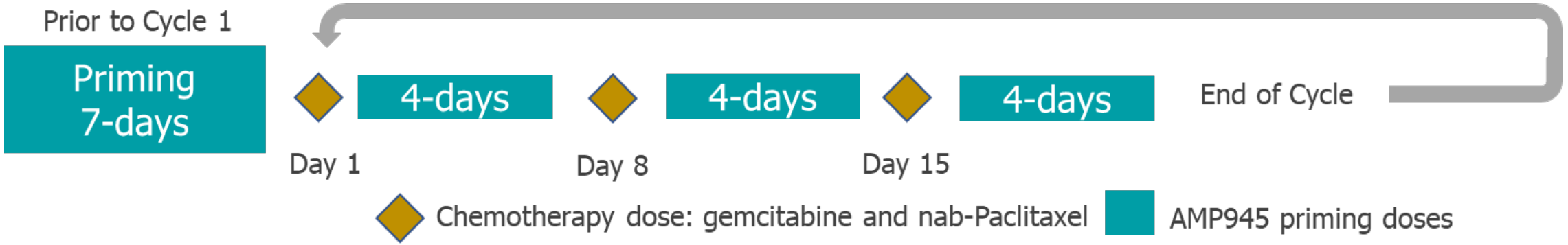
Phase 2 pancreatic cancer clinical trial "ACCENT"

- NCT05355298
- Dosing commenced in Q3 CY2022

- First-line therapy
  - Largest patient cohort
  - Healthier patients
  - Aims to position AMP945 as a first-line treatment option
- Patients with non-resectable or metastatic pancreatic cancer
- Intermittent dosing (priming) of AMP945 between normal chemotherapeutic doses of gemcitabine/nab-paclitaxel
  - Designed to enhance standard of care
  - Mirrors design of preclinical efficacy studies

ACCENT Priming Dose Regimen

- Amplia's Phase 1b/2a clinical trial AMP945-PC-201 (ACCENT, NCT05355298) will assess a pulse dosing regimen of AMP945 in combination with gemcitabine and nab-paclitaxel as first-line therapy in patients with unresectable or metastatic pancreatic cancer
- In ACCENT, patients will initially be treated with a one-week priming dose of AMP945 (once a day)
- Gemcitabine and nab-paclitaxel will be given according to a standard treatment regimen and the patients will be pulse dosed for four days AMP945 prior to weekly chemotherapy administration



ACCENT Clinical Trial Summary

Population

- Patients with Stage III or IV pancreatic cancer
- First line therapy
- ECOG status ≤ 1
- Life expectancy of >3 month

Design

- Phase 1b/2a open label, single arm study to evaluate safety, PK, PD and efficacy of AMP945 in combination with gemcitabine/nab-paclitaxel

Treatment

Dose escalation

- Fixed doses of G/A, escalating doses of AMP945
- 4 cohorts of 3-6 pts. 1 month cycle

Expansion

- Part 1: 26 pts
- Interim Analysis

Expansion

- Part 2: 24 pts

Endpoints

Dose Escalation

- Safety, PK, Optimal Dose

Expansion

- Primary: Objective response, duration of response
- Secondary: Overall survival, progression free survival
- Exploratory: Impact on/of biomarkers

Acknowledgements

Amplia

Amplia Team:

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- Rhiannon Jones
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- Adrian Sulisto
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- Mark Devlin
- John Lambert

Garvan Institute of Medical Research

Garvan Institute:

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- David Herrmann

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- Nicole Kruger

Nucleus Network:

- Jason Lickliter

- **Patients, families and caregivers involved in trials**
- **Amplia (ASX: ATX) Investors**
- **Funding bodies:** NHMRC, ARC, Cancer Council NSW, Cancer Institute NSW, Cancer Australia, Tour de Cure, St. Vincent's Clinic Foundation, PanKind

PanKind The Australian Pancreatic Cancer Foundation

Cancer Council NSW

Tour de Cure