Amplia
THERAPEUTICS

Focal Adhesion Kinase Inhibitors:
Targeting Cancer and Fibrosis

June 2024

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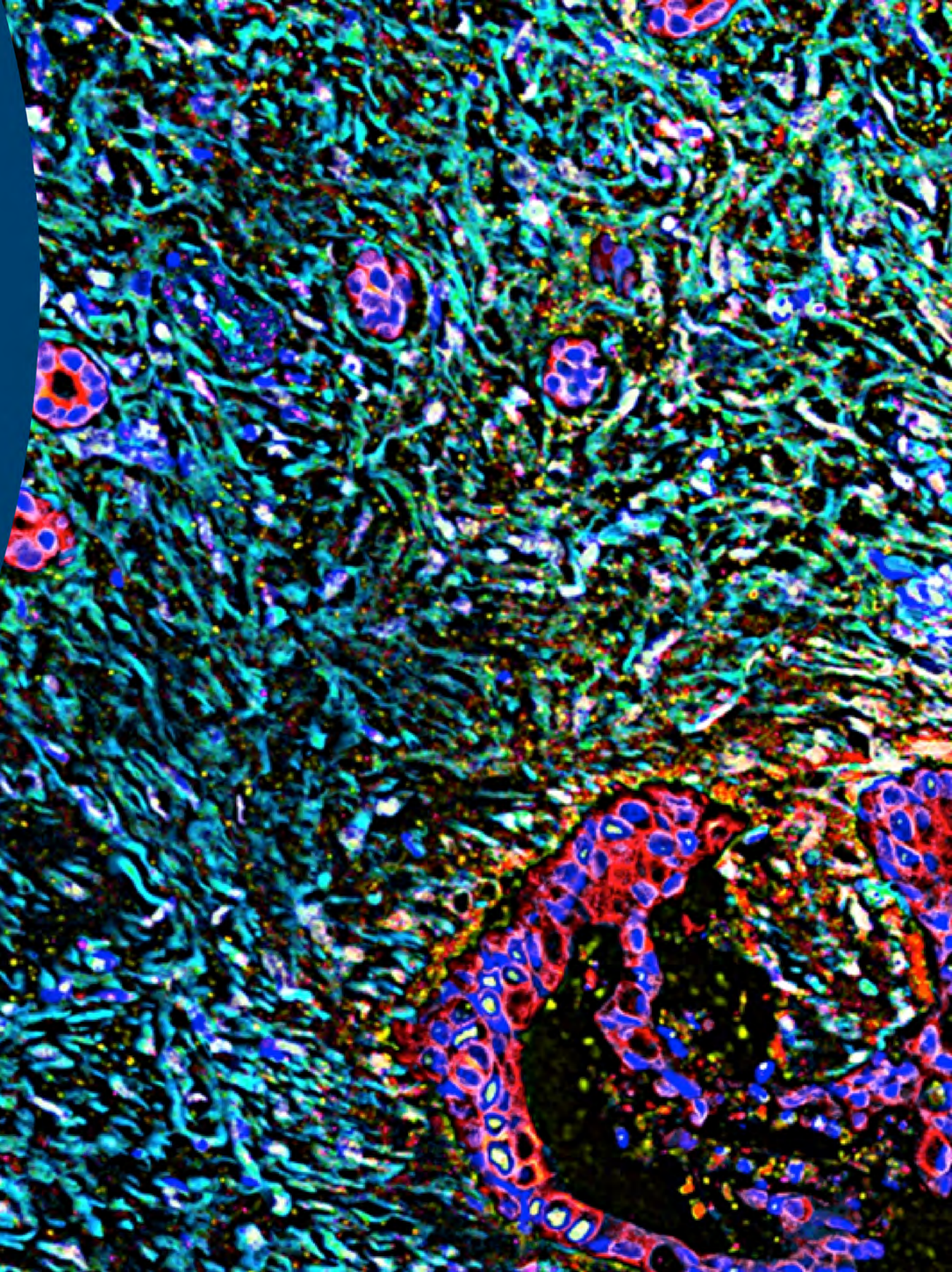

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Outline

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Section Two
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Section Three
Narmafotinib in Solid Tumours

Section Four
Narmafotinib in the Clinic

Section Five
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Section One

Corporate Overview

Amplia THERAPEUTICS

COMPANY OVERVIEW

- ASX:ATX
- Headquartered in Melbourne, Australia
- Market capitalization: A$19.6M
- AU Institutional Investors include Platinum, Blueflag, Acorn Capital, Pengana Capital

BOARD OF DIRECTORS

Warwick Tong
MB ChB MPP GAICD
Chair
Senior and executive roles at GSK, Surface Logix, Cancer Therapeutics CRC

Robert Peach
PhD
Director
Senior drug development roles at Apoptos, Biogen Idec, IDEC, BMS, Receptos

Jane Bell
AM, LLB, LLM (Lond), FAICD
Director
Banking and finance lawyer; experienced Board member incl. Mesoblast and Monash Health

Chris Burns
PhD, GAICD
CEO and MD
Experienced drug R&D leader: Pfizer, Cytopia, YM BioSciences, Gilead

HIGHLIGHTS

Clinical trial in advanced pancreatic cancer underway

- Interim readout planned for Q3 2024
- Preliminary signs of efficacy

Lean, experienced drug development team

- Network of experienced consultants and contractors

Open IND for narmafotinib trial in pancreatic cancer

Orphan Drug Designation for pancreatic cancer and IPF

Compelling preclinical data in disease models:

- Pancreatic cancer
- Ovarian cancer
- Idiopathic Pulmonary Fibrosis (IPF)

PIPELINE

Drug	Target	Indication	Preclinical	IND enabling	Phase 1	Phase 2	Late Phase	Status
ONCOLOGY								
Narmafotinib (AMP945)	**FAK**	Pancreatic Cancer (+Gemcitabine/Abraxane)			ACCENT			Enrolling
		Pancreatic Cancer (+FOLFIRINOX)						IND approved
		Ovarian Cancer						In planning
		Other solid tumours						
AMP886	**FAK/VEGFR3/FLT3**	Solid tumours						
FIBROTIC DISEASE								
Narmafotinib (AMP945)	**FAK**	Idiopathic Pulmonary Fibrosis						
		Other fibrotic diseases						
TOPICAL								
Narmafotinib (AMP945)	**FAK**	Scar Reduction						POC developed

next 12 months

MILESTONES

	2024	2025	
Pancreatic Cancer	ACCENT Interim Analysis	Commence FOLFIRINOX Trial in US	ACCENT Trial Complete; Phase 2b/3 Planning
Ovarian Cancer		Commence Clinical Trial	
Partnering			Regional Licensing Deal

Section Two

FAK and Narmafotinib

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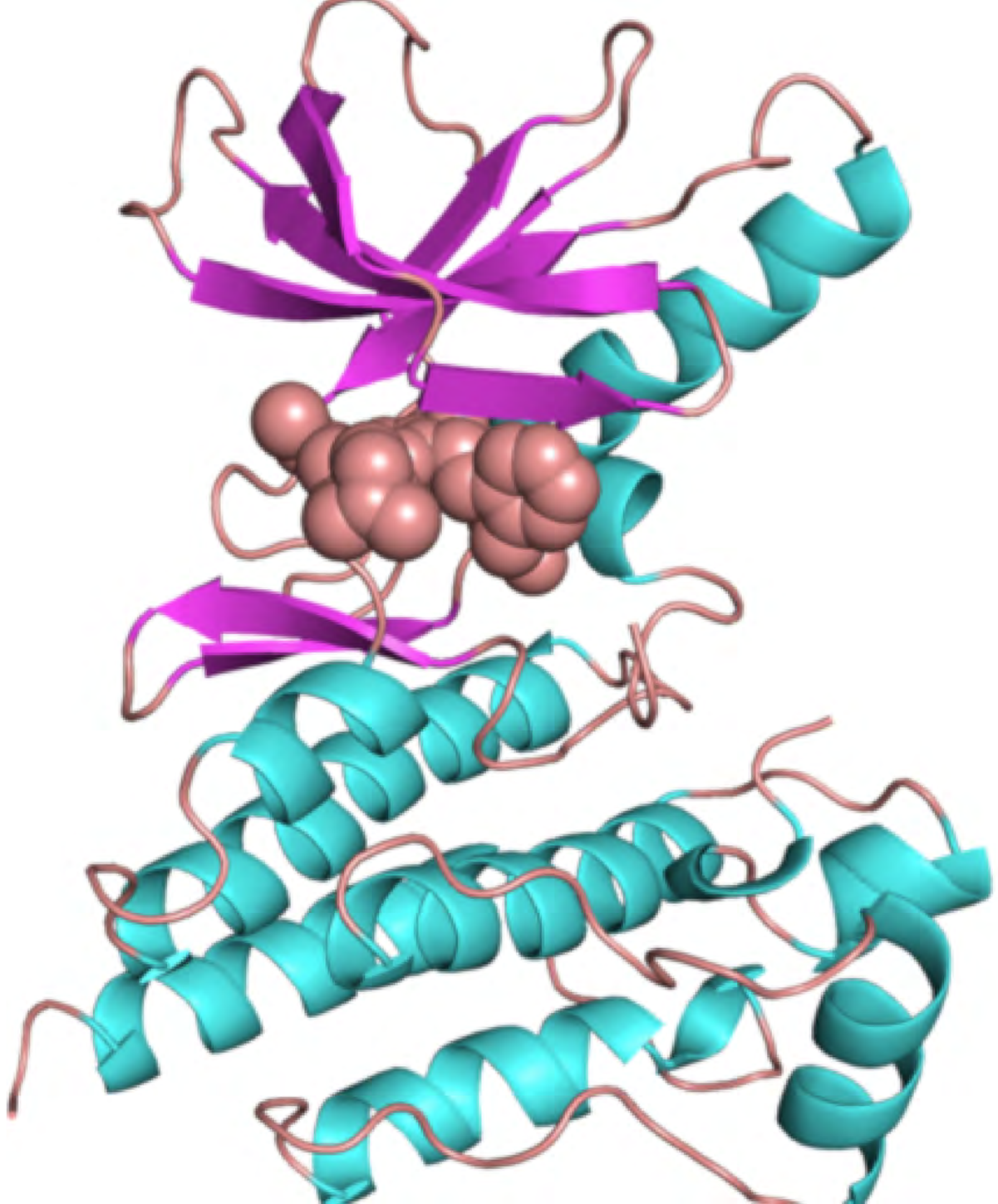


ROLE OF FAK IN CANCER

FAK involvement in **both cell intrinsic and extrinsic effects** allows an inhibitor to target multiple cancer pathways. A FAK inhibitor is well placed to work in combination with various combination therapies and in multiple indications.

Target:

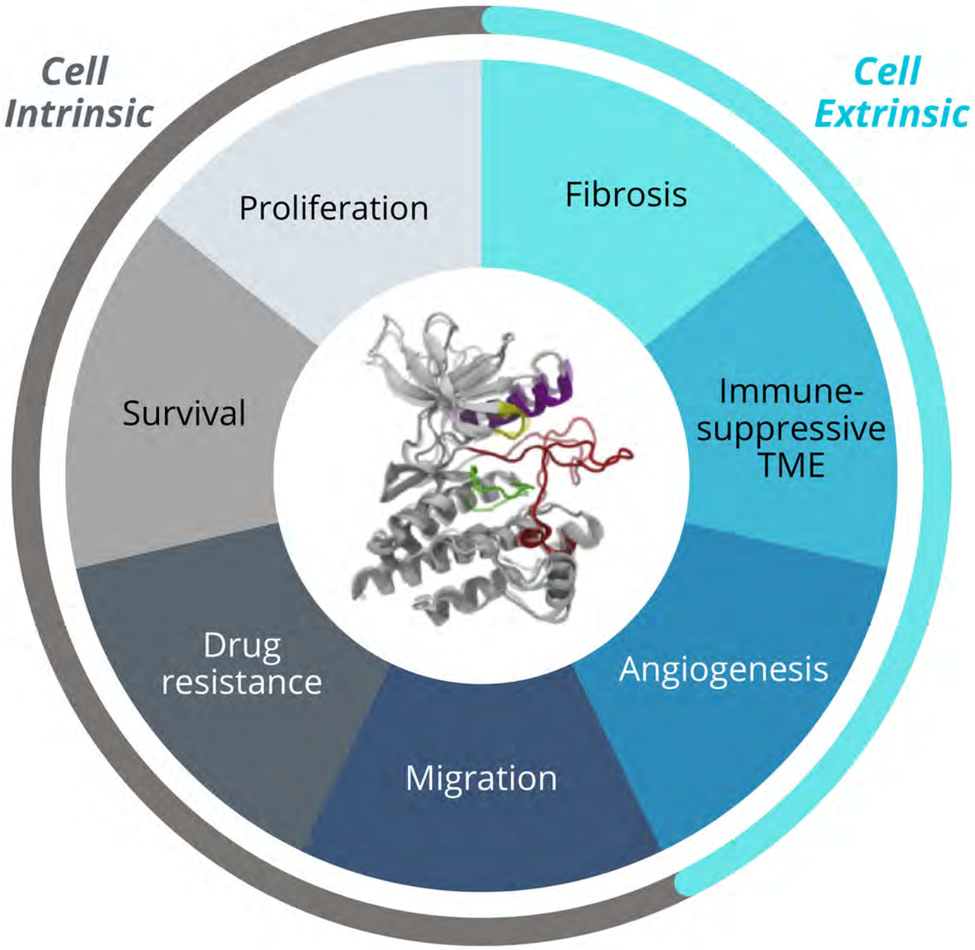
- Cell proliferation and migration
- Chemoresistance
- TME desmoplasia
- Suppression of immune response

Combination therapy:

- Standard of care chemotherapies
- Targeted therapies
- Immunotherapies
- Radiotherapy

Indications:

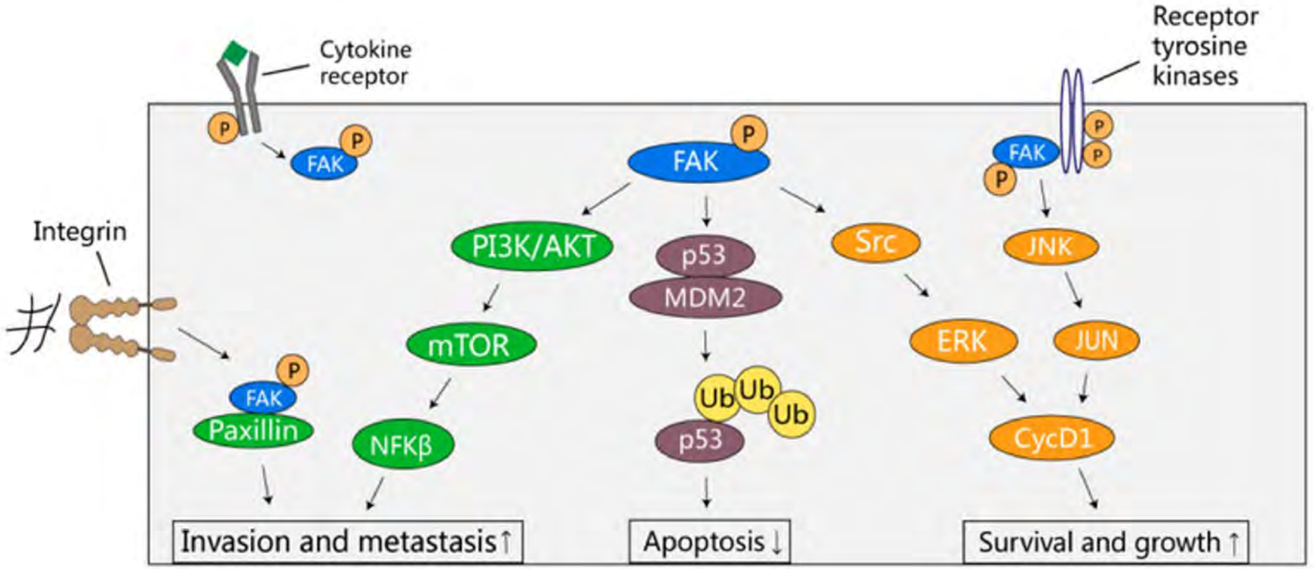
- Pancreatic cancer
- Ovarian cancer
- Cholangiocarcinoma
- Liver cancer
- Gastric Cancer
- Others...



POTENTIAL FOR COMBINATION WITH TARGETED AGENTS

Literature evidence for synergistic or additive combinations with:

- Raf/Mek inhibitors
- Kras inhibitors
- Hippo Pathway inhibitors
- I/O agents
  - anti PD-1 and PD-L1
  - anti-TIGIT
  - T cell co-stimulators



Disc. Oncol. 2021, 12, 52

NARMAFOTINIB (AMP945)

Drug-like, ATP-competitive, small molecule

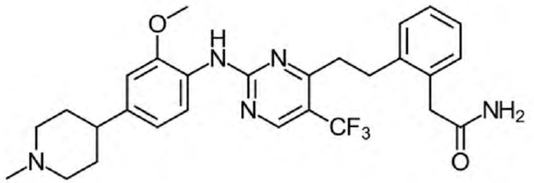
Highly potent and selective

Excellent PK; once-a-day dosing

Minimal risk for drug-drug interactions

Best-in-class profile

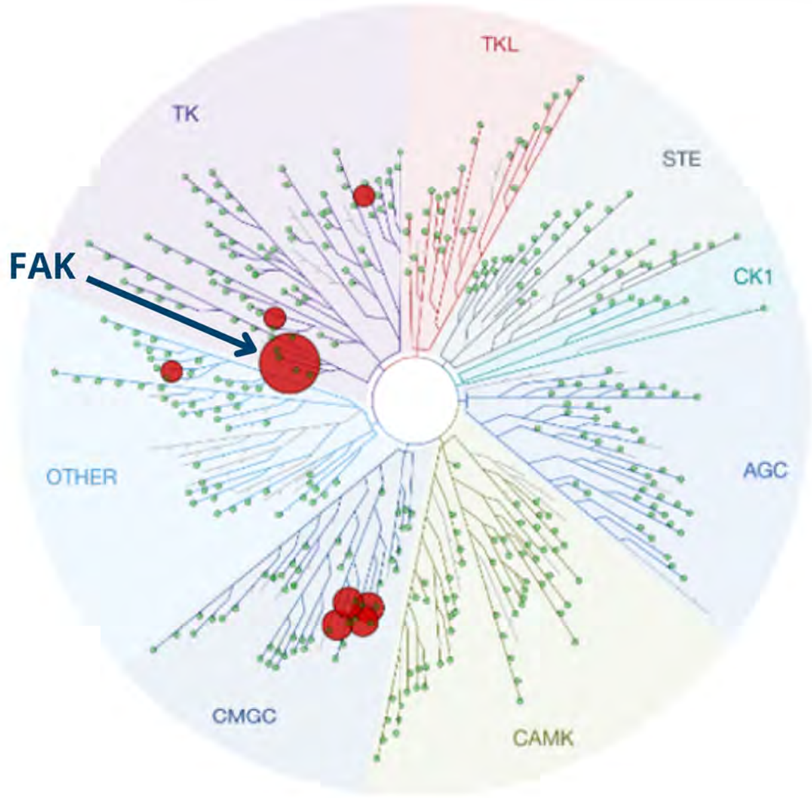
Narmafotinib
Drug-like small molecule



FAK Activity
Highly potent FAK inhibitor

IC_{50}	2.2 nM
K_D	29 pM

Selectivity
Highly selective for FAK



Section Three

Narmafotinib in Solid Tumours

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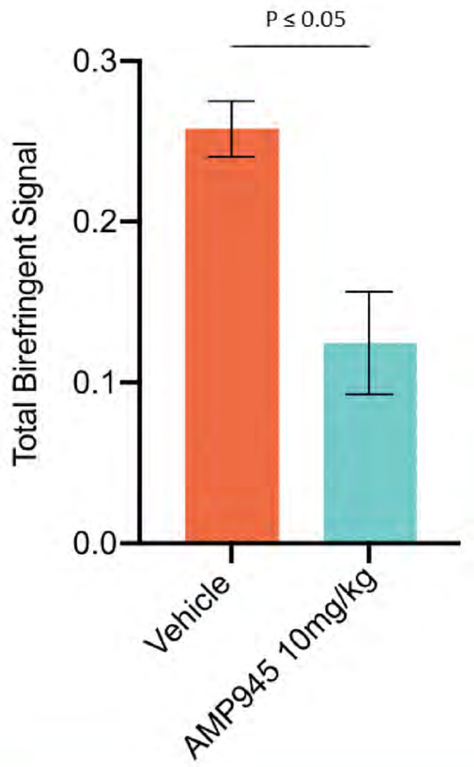
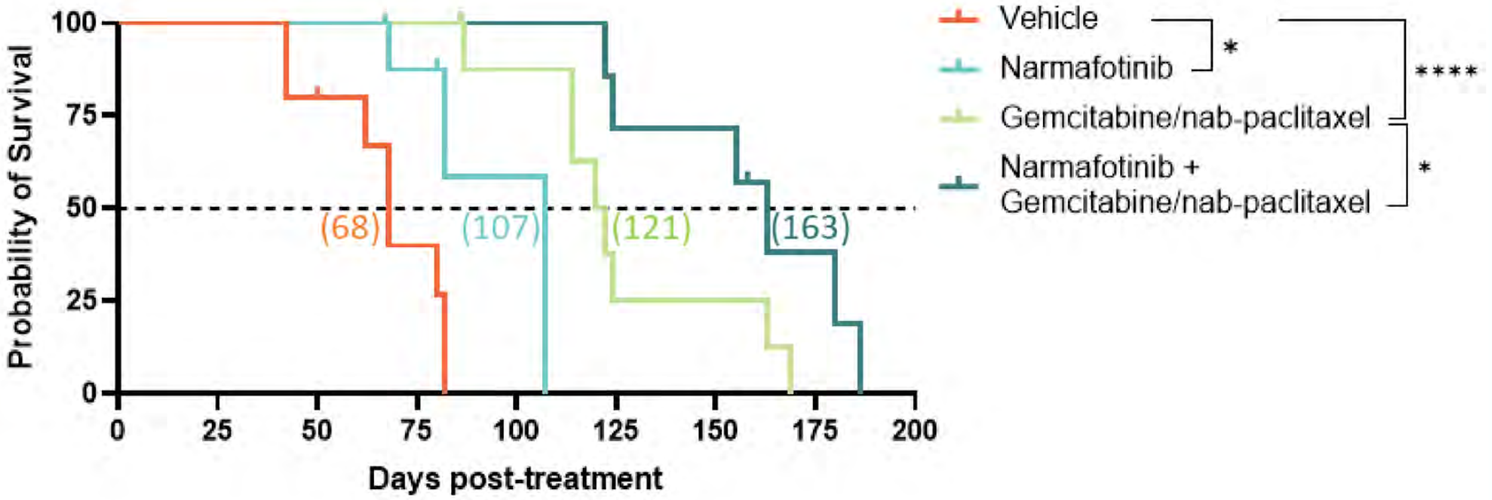
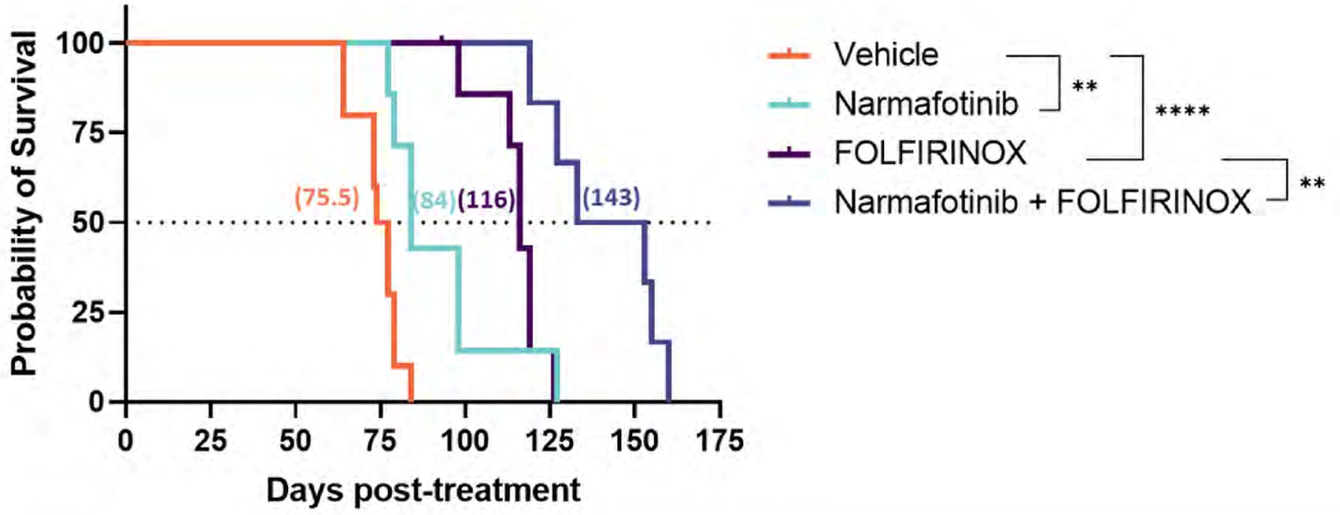
NARMAFOTINIB ACTIVITY IN VIVO

Reduces total collagen



Increases Survival



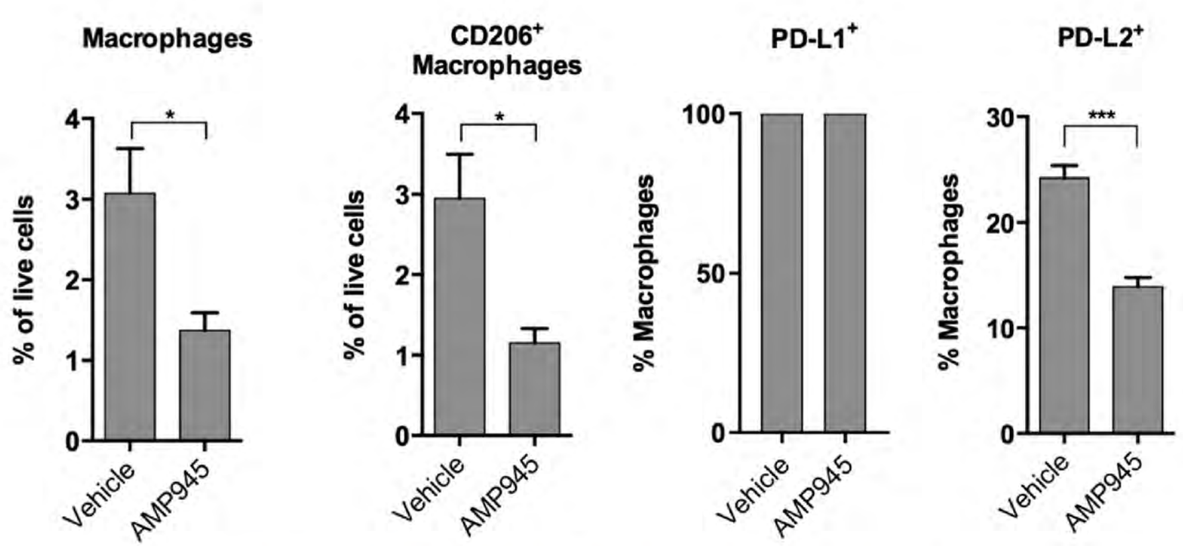


Garvan Institute of Medical Research

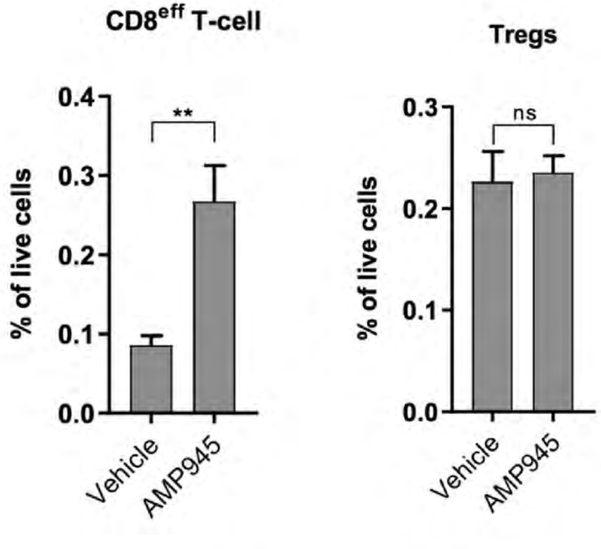
Timpson Lab (Garvan Institute)

NARMAFOTINIB INCREASES IMMUNO-REACTIVITY OF TME

In vivo, narmafotinib treatment reduces tumor-infiltrating MDSCs* and tumor-associated macrophages and increases CD8+ T-cells



Effects on Tumor Associated Macrophages



Effects on T cells

SCC mouse model; Narmafotinib (80 mg/kg, p.o. q.d.)
Tumors excised day 12 for analysis

* Myeloid derived suppressive cells

Frame Lab (Uni of Edinburgh)

(Serrels et al., 2015, Cell 163, 160–173)

Section Four

Narmafotinib in the Clinic

PHASE 1 TRIAL OF NARMAFOTINIB

Trial Execution

Recruited 56 healthy volunteers aged 18 – 65

Single and multiple ascending doses

Single site in Melbourne, Australia

Completed 2021

Summary of Outcomes

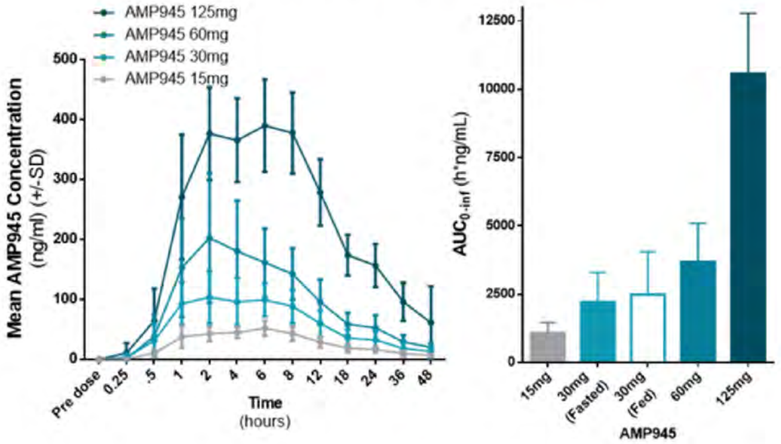
Safe and well-tolerated at all doses tested

- No serious adverse events (SAEs) or withdrawals and no identified safety trends

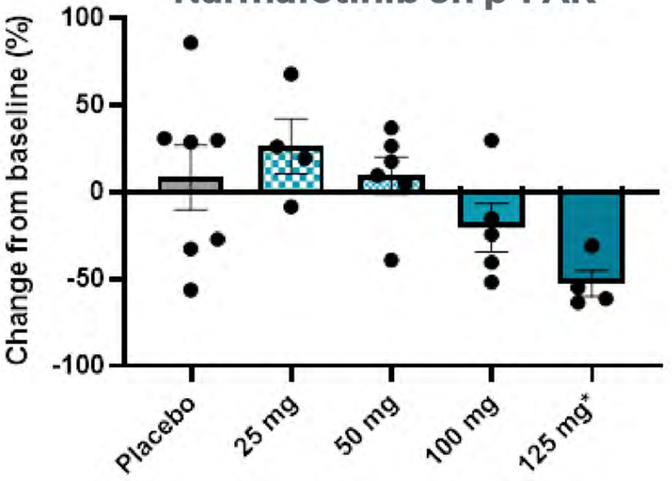
Once-a-day oral dose supported by pharmacokinetics

Inhibition of FAK demonstrated in skin biopsies taken from participants (pFAK levels decrease with increasing dose)

Pharmacokinetics in Single Ascending Dose Study



Pharmacodynamic effect of Narmafotinib on p-FAK



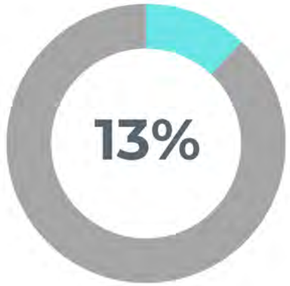
Registry number: ACTRN12620000894998

PANCREATIC CANCER

Increasing Prevalence

Est. 64,000 diagnoses and 50,000 deaths in US this year*

4,500 were diagnosed in 2023 in AU in 2023**



5 year survival

Difficult-to-treat: typically detected late in disease progression

Market size

Global treatment market estimated over US$6 billon in 2023

Projected to grow to ~US$36 billion by 2036†

* American Cancer Society (link)
** Cancer Australia (link)

† Research Nester (link)

ACCENT PHASE 1B/2A CLINICAL TRIAL

First-line therapy

Patients with non-resectable or metastatic pancreatic cancer

Intermittent dosing of narmafotinib between normal chemotherapeutic doses of gemcitabine/nab-paclitaxel

- Designed to enhance standard of care
- Mirrors design of preclinical efficacy studies

Phase 1b: Dose Selection
Phase 2a: Simon's 2 Stage design with 50 patients

Overall Endpoints:

- Primary
  - Objective response rate
  - Duration of response
- Secondary
  - Overall survival
  - Progression free survival
- Exploratory
  - Impact on/of biomarkers

G/A = gemcitabine/Abraxane (nab-paclitaxel)

ClinicalTrials.gov NCT05355298

ACCENT TRIAL DESIGN

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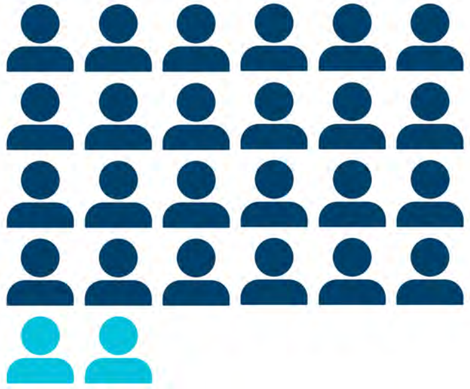
Phase 1b → **Dose Selected** → **Phase 2a** → **Interim Analysis** → **Phase 2a (cont)**

14 patients

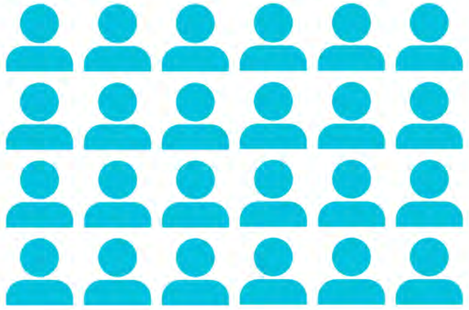
COMPLETED

26 patients



RECRUITING

24 patients



ACCENT PHASE 1B SUMMARY

3 Cohorts (100 mg, 200 mg, 400 mg; QD)

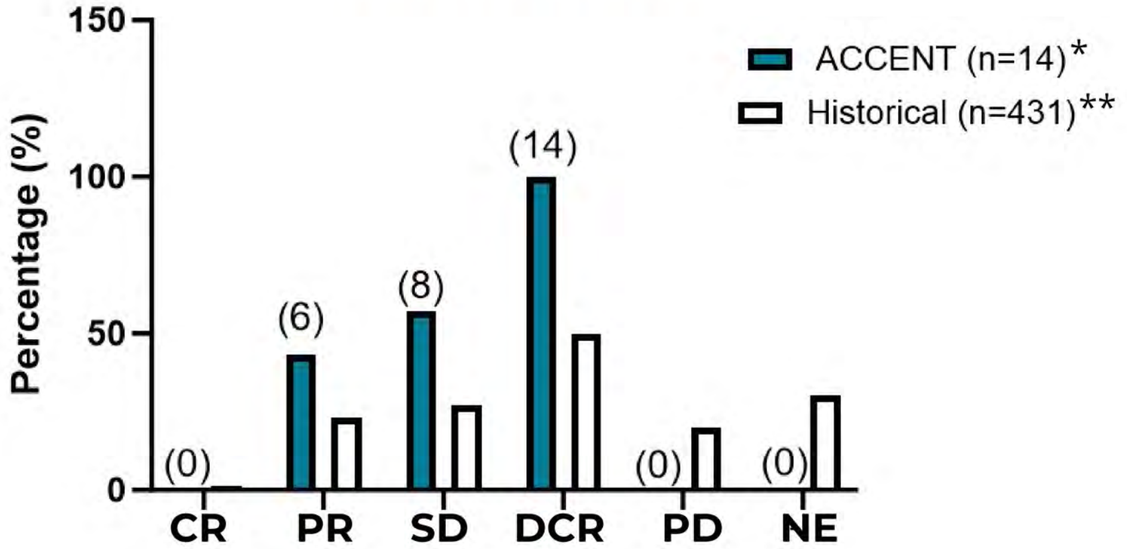
Safe and well tolerated

- All patients elected to stay on drug post cycle 1
- One DLT: uncontrolled nausea
- Fatigue (Gr 3 or below) in more than 1 patient likely drug related

Comparison to historical gemcitabine/Abraxane combination

- Includes patients on all doses
- Not powered for efficacy
- 9 of 14 patients on drug > 5 months

Best Response - all patients Phase 1b Trial



CR - Complete Response

PR - Partial Response (reduction in tumour size >30%)

SD - Stable Disease

DCR - Disease Control Rate (PR +SD)

PD - Progressive Disease

NE - Not Evaluable

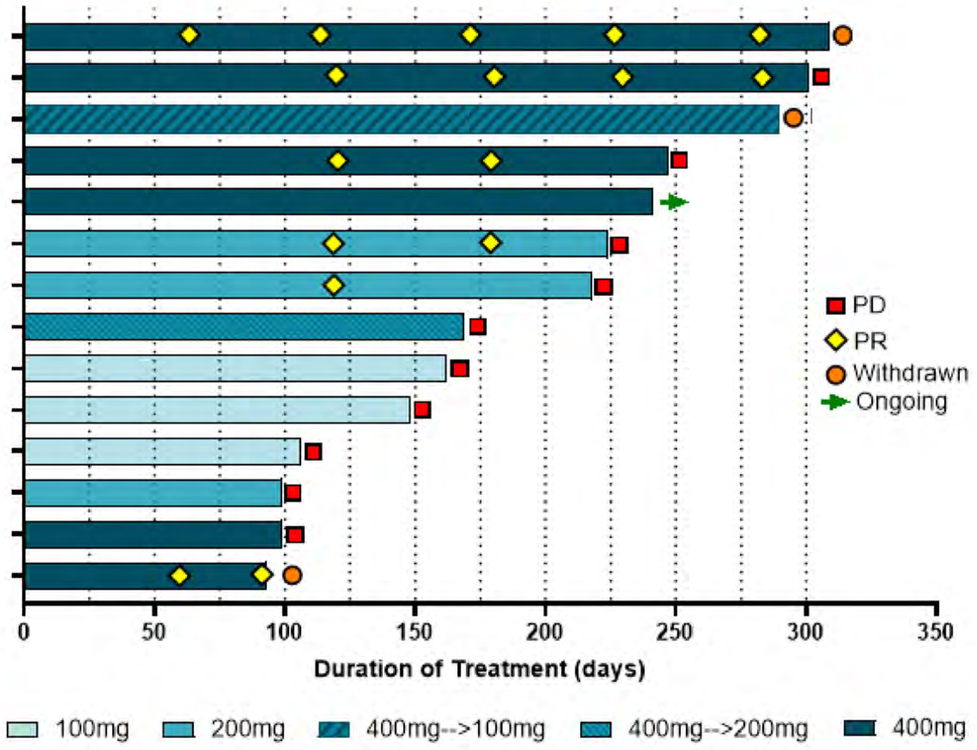
* Investigator reviewed

** Independent review as part of MPACT trial (NEJM 2013: 369; 1691-1703)

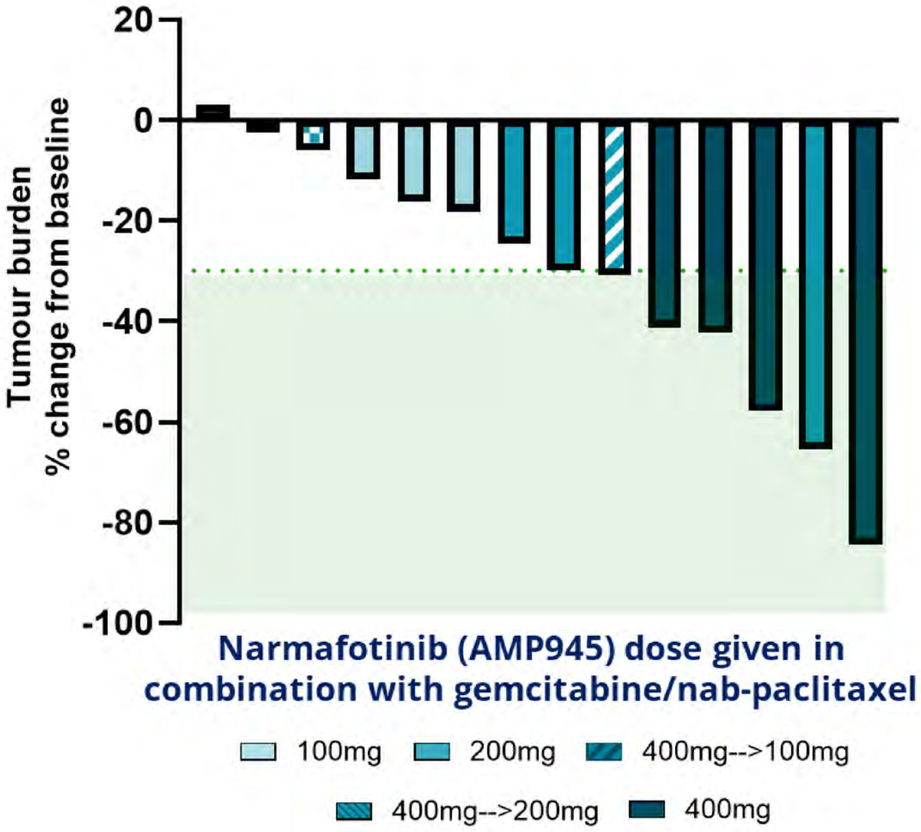
NB. Phase 1b trial not powered for efficacy

ACCENT PHASE 1B SUMMARY

Patient Duration on ACCENT trial
(as at May 2024)



Best response
(as at May 2024)



Section Five

Summary

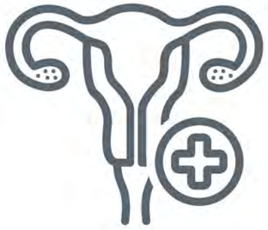
OPPORTUNITY SUMMARY

Combinations in pancreatic cancer

Gemcitabine and Abraxane (ACCENT trial)

-

FOLFIRINOX (US trial with open IND)



Combinations in ovarian cancer

Platinum resistant disease

-

Maintenance therapy post surgery

Preclinical evidence in other solid tumors

Bile duct, oesophageal, head and neck cancer

-

kRAS-mutant cancers (e.g. lung, colorectal)

-

Other fibrotic cancers (e.g. liver cancer)

COMPETITIVE ADVANTAGE

	Selectivity	Good PK profile	Good DDI profile	Clinical Notes	Stage of development
Narmafotinib	✓	✓	✓	**Safe and well tolerated**	**Phase 1b/2a (pancreatic cancer)**
Defactinib (Verastem)	✗	✗	?	Recent success in Phase 2 LGSOC	Phase 2 pancreatic & ovarian cancer trials in combination with PD1 or RAF/MEK inhibitors
Ifebemtinib (Inxmed)	✓	✓	?	Drug related, off-target adverse events noted	Phase 2 (ovarian cancer) Phase 1b/2 in KRAS mutant solid tumours
GSK2256098	✓	✗	✗	First generation FAKi Issues with DDI and MTD lower than effective dose	DISCONTINUED

HIGHLIGHTS

- Best-in-class
- Orphan drug designation in pancreatic cancer and IPF
- Demonstrated safety and tolerability in healthy volunteers and patient population
  Preliminary signs of efficacy in pancreatic cancer
- Open IND
- Strong IP position

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THERAPEUTICS

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