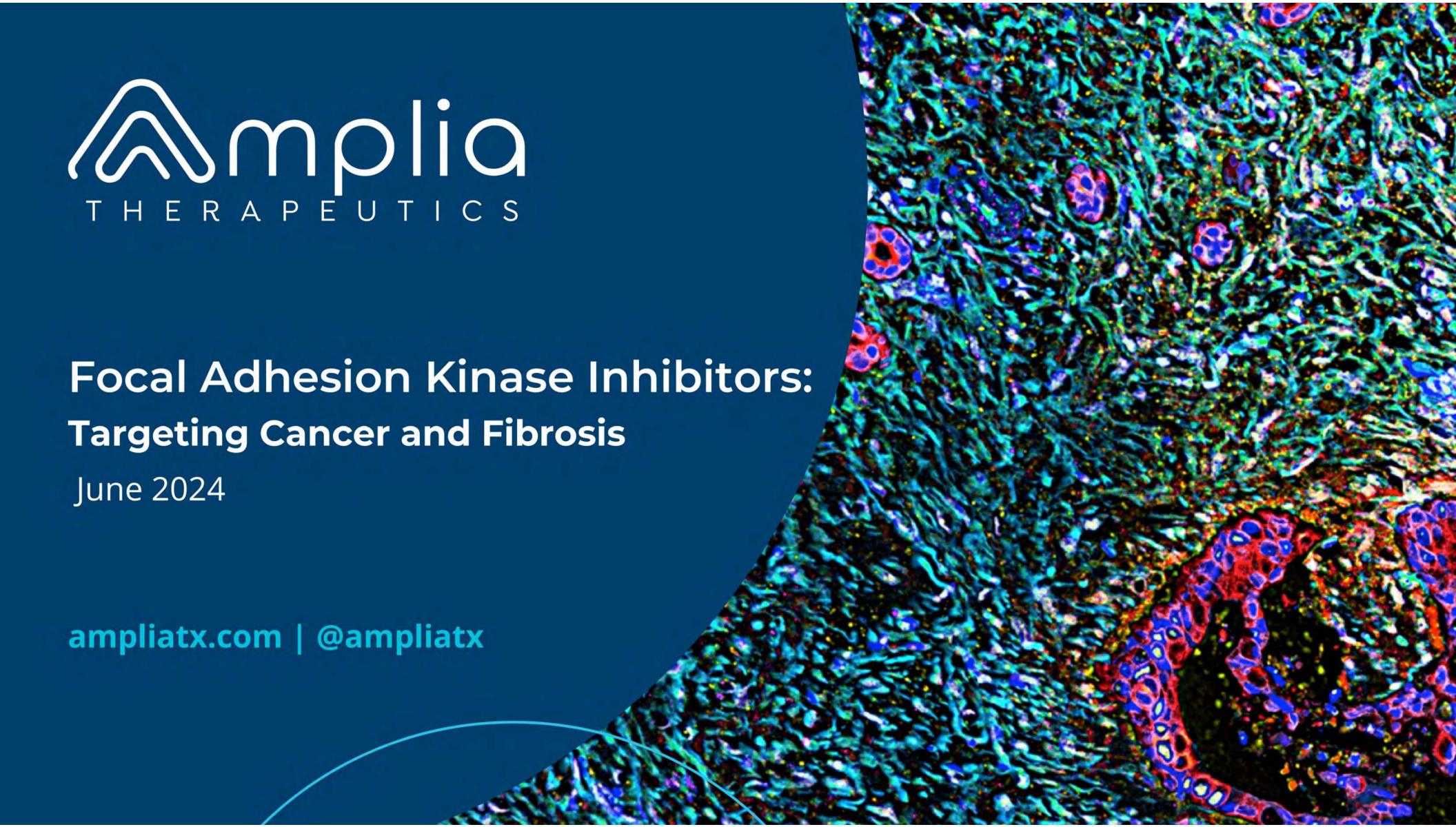
Amplia THERAPEUTICS

# Focal Adhesion Kinase Inhibitors:

## Targeting Cancer and Fibrosis

June 2024



ampliatx.com | @ampliatx

# Important Notice and Disclaimer

This presentation (**Presentation**) contains summary information about Amplia Therapeutics Limited ACN 165 160 841 and its subsidiaries (the **Company** or **Amplia**) which is current as at 31 Mar 2024. By attending an investor presentation or briefing, or accepting, accessing or reviewing this Presentation, you acknowledge and agree to the terms set out below.

**Summary Information:** This Presentation has been prepared for information purposes only and is a summary only. It should be read in conjunction with Amplia's most recent financial report and other periodic and continuous disclosure information lodged with the Australian Securities Exchange (ASX), which is available at www.asx.com.au. Subject only to any legal obligation to do so, the Company does not have any obligation to correct or update the content of this Presentation.

**Not financial product advice:** This Presentation does not, and does not purport to, contain all information necessary to make an investment decision, is not intended as investment or financial advice (nor tax, accounting or legal advice) and must not be relied upon as such. This Presentation does not take into account the investment objectives, financial situation or needs of any particular investor. Investors are encouraged to seek independent professional advice when deciding if an investment in the Company is appropriate. The Company is not licensed to provide financial product advice in respect of its own securities. This Presentation is not a prospectus, product disclosure statement or other offering document under Australian law (or any other law). It is not, and does not constitute, an invitation or offer of securities for subscription, purchase or sale in any jurisdiction.

**Investment risk and past performance:** An investment in Amplia shares is subject to known and unknown risks, some of which are beyond the control of the Company and its directors. The Company does not guarantee any particular rate of return or the performance of Amplia. Past performance is not, and should not be relied on as being, indicative of future performance.

**Future performance and forward-looking statements:** This Presentation includes forward looking statements, which can generally be identified by the use of words such as "may", "will", "expect", "intend", "plan", "estimate", "anticipate", "outlook", "forecast" and "guidance", or other similar words. They may include, without limitation, statements regarding plans, strategies and objectives and anticipated business developments. Forward-looking statements inherently involve known and unknown risks, uncertainties and other factors that may cause Amplia's actual results, performance and achievements to differ materially from statements in this Presentation. Forward-looking statements are based on the Company's good faith assumptions as to the financial, market, regulatory and other relevant environments that will exist and affect Amplia's business and operations in the future. The Company does not give any assurance that the assumptions will prove to be correct. There may be other factors that could cause actual results or events not to be as anticipated, and many events are beyond the reasonable control of the Company. Readers are cautioned not to place undue reliance on forward-looking statements. Forward-looking statements in this Presentation are only made as at the date of this Presentation and the Company does not undertake any obligation to publicly update or revise any of the forward-looking statements or to advise of any change in assumptions on which any such statement is based.

**Industry data and third party information:** Industry data and third party information used in this Presentation may have been obtained from research, surveys, reports or studies conducted by third parties, including industry or general publications. Neither Amplia not its representatives have independently verified any such market or industry data.

**Financial Information:** This Presentation contains historical financial information based on the Company's results for the 12 month period ending 31 March 2024. All financial information disclosed in this Presentation is presented in Australian dollars unless otherwise noted. Any discrepancies between totals and sums of components in tables and figures contained in this Presentation are due to rounding.

**Disclaimer:** To the maximum extent permitted by law, Amplia and its officers, directors, employees, agents and advisers: (1) disclaim all responsibility and liability (including, without limitation, any liability arising from fault, negligence or negligent misstatement) for any loss arising from this Presentation or reliance on anything contained in or omitted from it or otherwise arising in connection with this Presentation; (2) disclaim any obligation or undertaking to release any update or revision to the information in this Presentation to reflect any change in expectations or assumptions; and (3) do not make any representation or warranty, express or implied, as to the accuracy, reliability, completeness of the information in this Presentation or that this Presentation contains all material information about Amplia or that a prospective investor or purchaser may require in evaluating a possible investment in Amplia or acquisition of shares, or the likelihood of fulfilment of any forward-looking statement.

# Outline

**Section One**
Corporate Overview

**Section Two**
FAK and Narmafotinib

**Section Three**
Narmafotinib in Solid Tumours

**Section Four**
Narmafotinib in the Clinic

**Section Five**
Summary

Amplia THERAPEUTICS

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

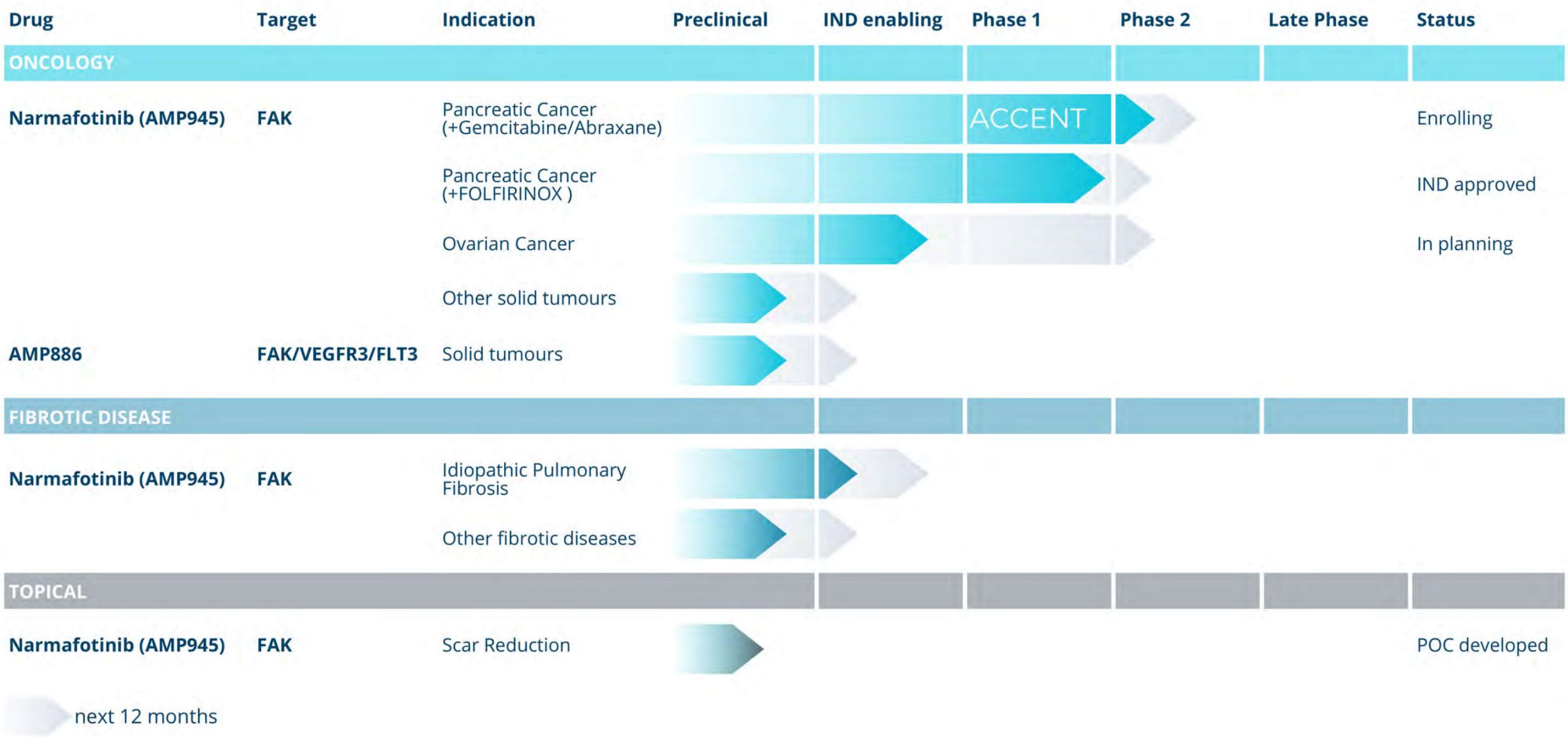
**Open IND for narmafotinib trial in pancreatic cancer**

**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

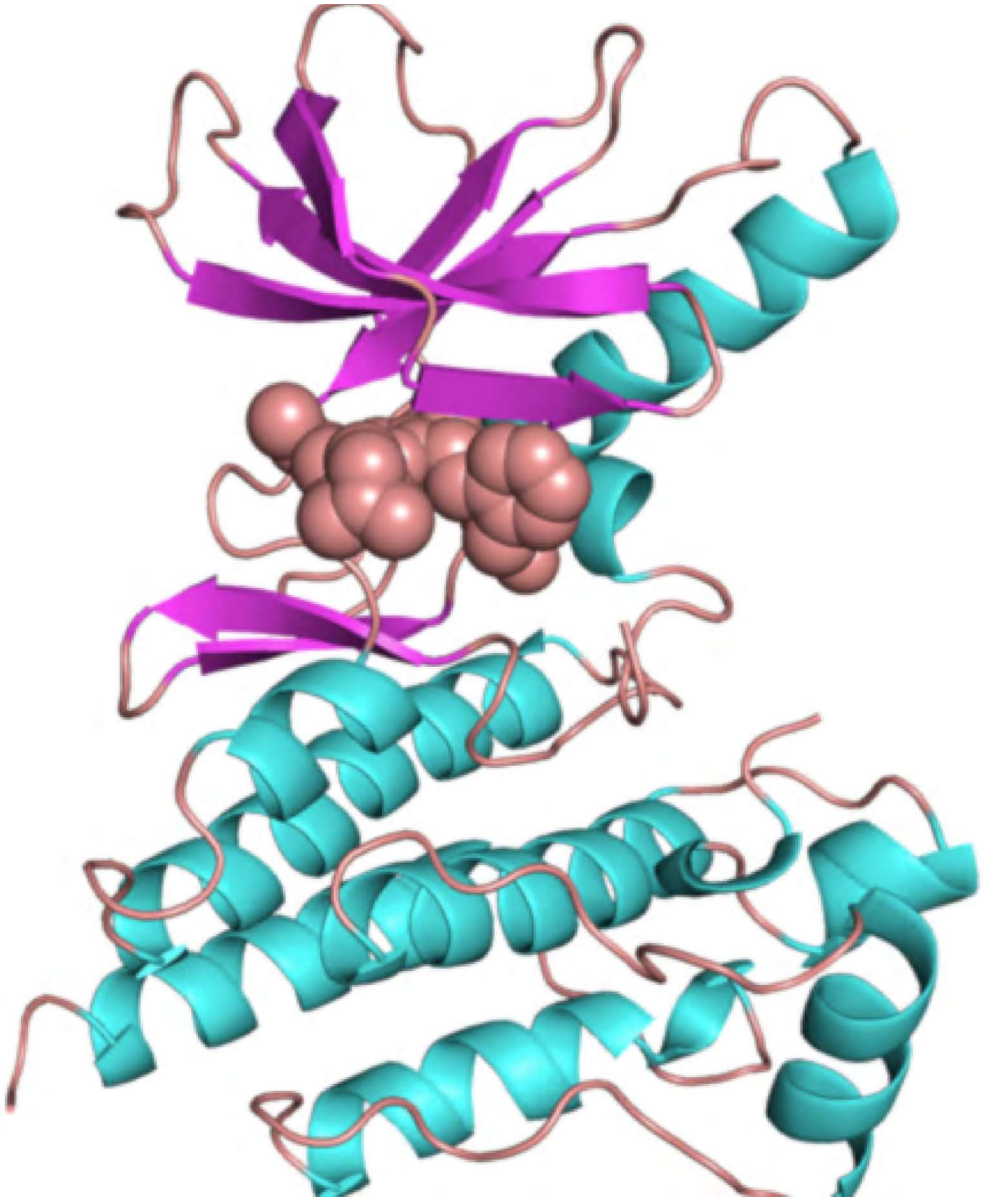
# MILESTONES


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

Amplia THERAPEUTICS



# 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:

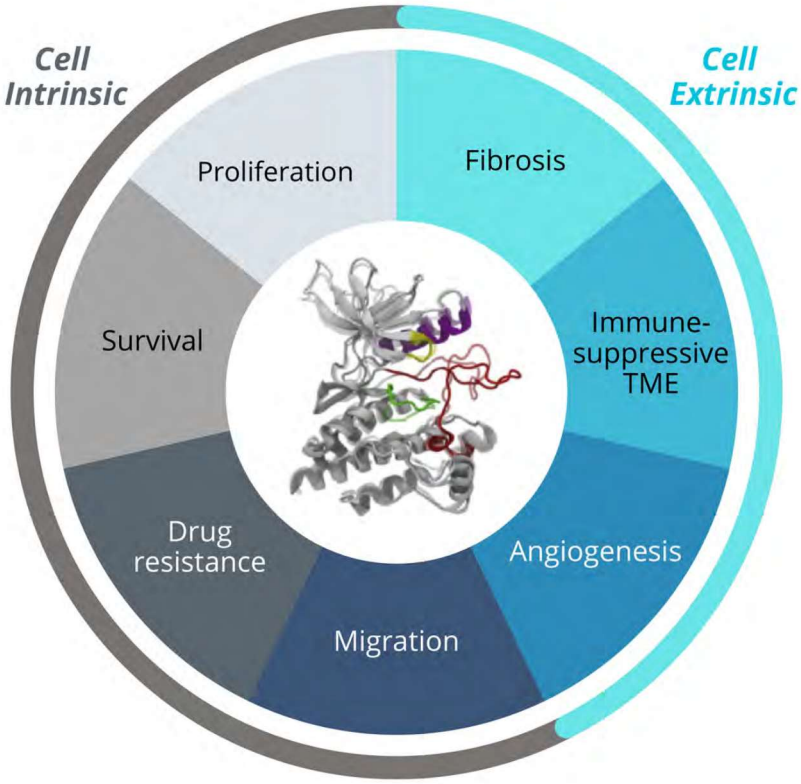
- Cell proliferation and migration
- Chemoresistance
- TME desmoplasia
- Suppression of immune response

Combination therapy:

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

Indications:

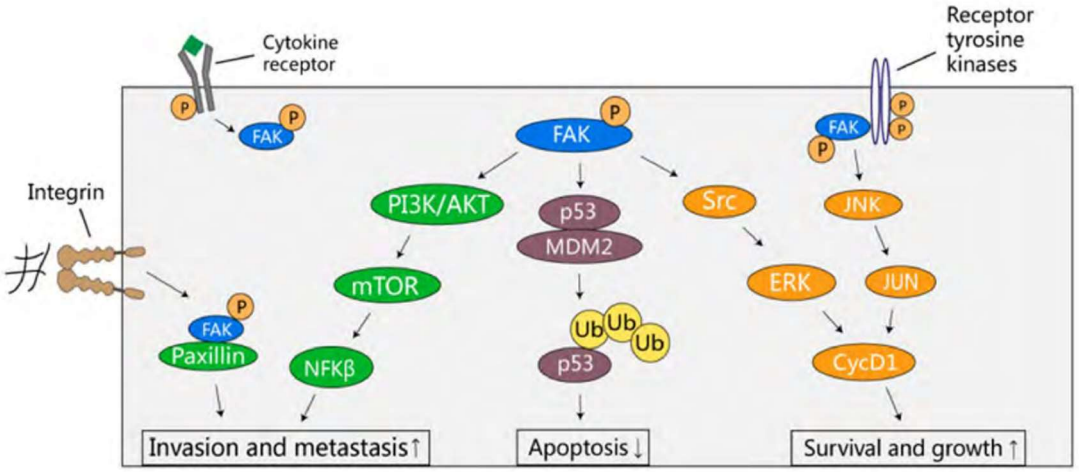
- Pancreatic cancer
- Ovarian cancer
- Cholangiocarcinoma
- Liver cancer
- Gastric Cancer
- Others...



# 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

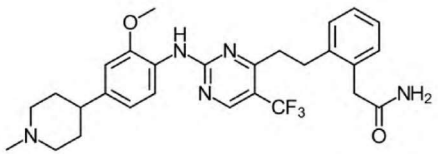
Highly potent and selective

Excellent PK; once-a-day dosing

Minimal risk for drug-drug interactions

Best-in-class profile

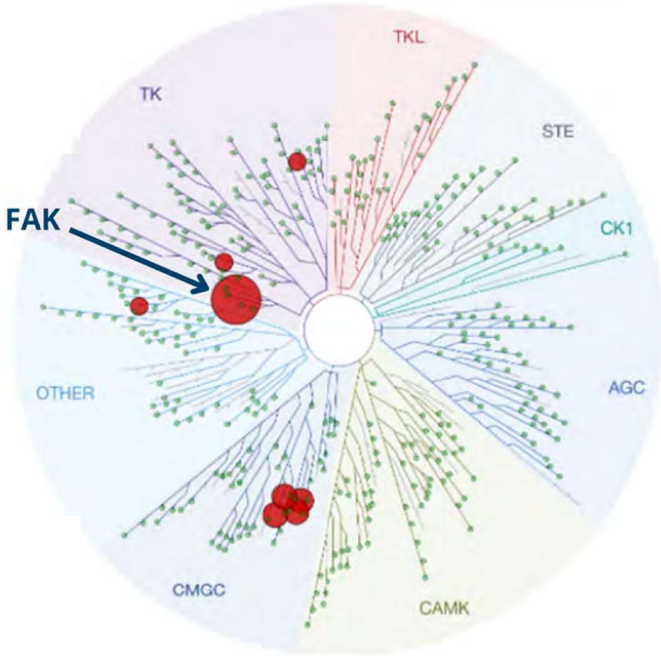
**Narmafotinib**
Drug-like small molecule



**FAK Activity**
Highly potent FAK inhibitor

| | |
|---|---|
| $IC_{50}$ | 2.2 nM |
| $K_D$ | 29 pM |

**Selectivity**
Highly selective for FAK



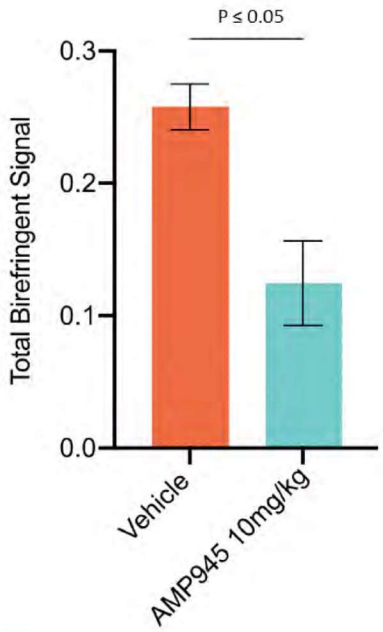
Section Three

# Narmafotinib in Solid Tumours

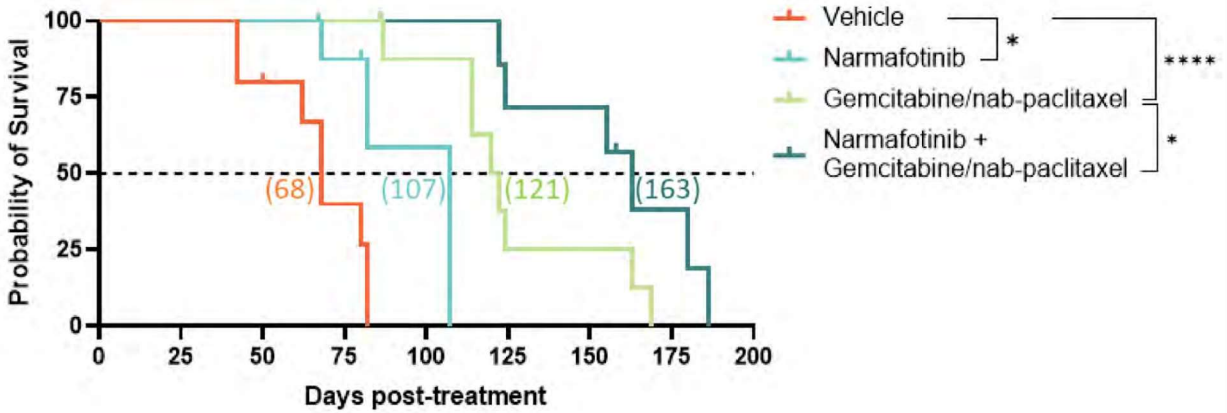
Amplia THERAPEUTICS

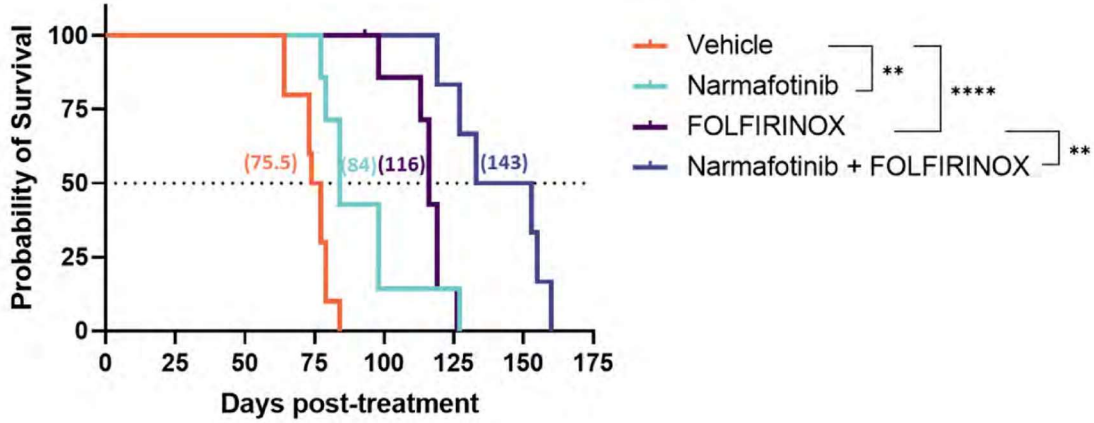
# NARMAFOTINIB ACTIVITY IN VIVO

## Reduces total collagen




## Increases Survival



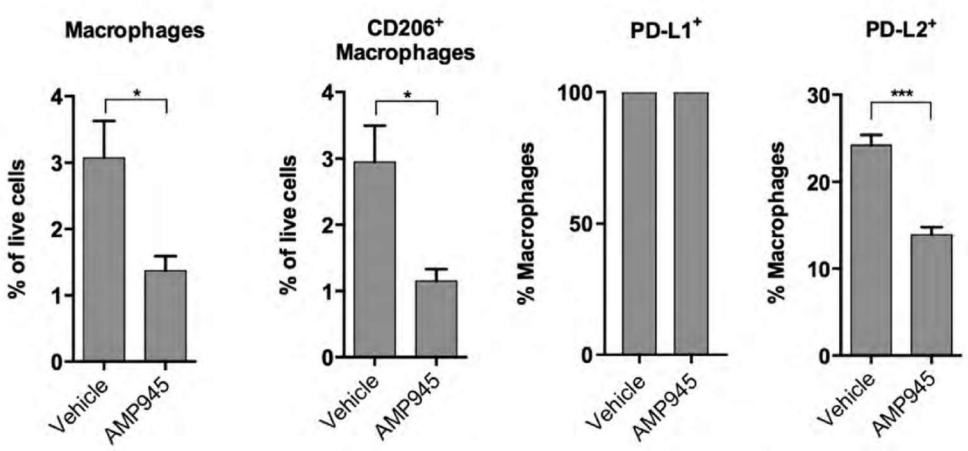




Garvan Institute of Medical Research

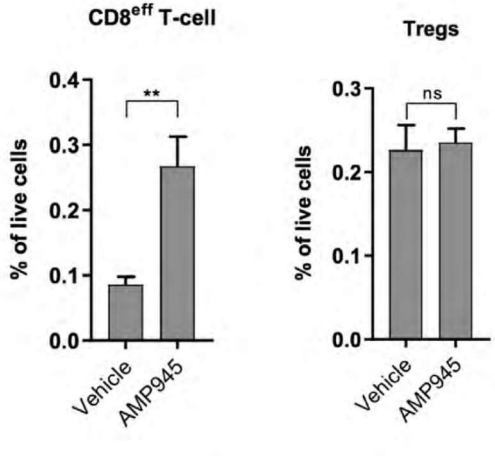
*Timpson Lab (Garvan Institute)*

# 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

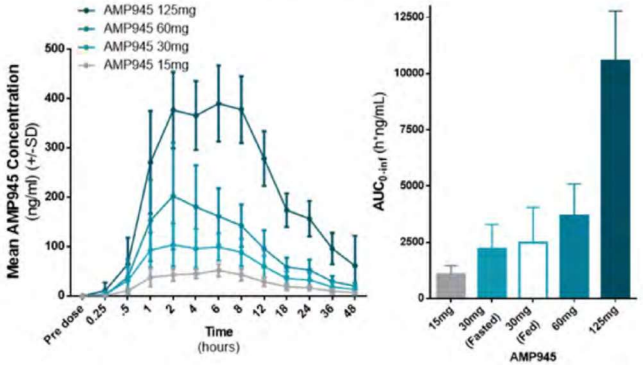
Safe and well-tolerated at all doses tested

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

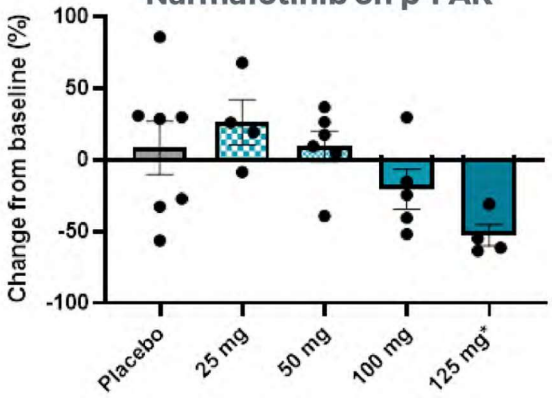
Once-a-day oral dose supported by pharmacokinetics

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

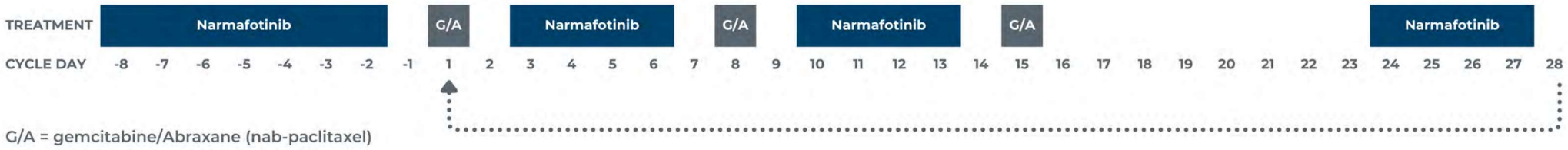
Intermittent dosing of narmafotinib between normal chemotherapeutic doses of gemcitabine/nab-paclitaxel

- 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)

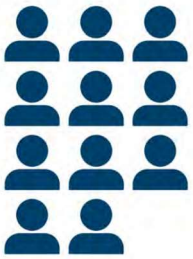
ClinicalTrials.gov NCT05355298

# ACCENT TRIAL DESIGN

Amplia THERAPEUTICS

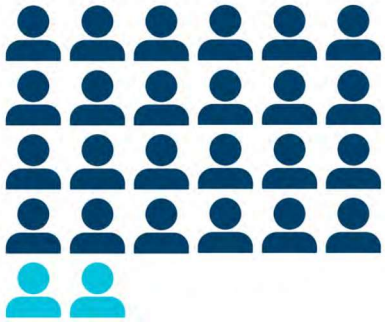
**Phase 1b** → **Dose Selected** → **Phase 2a** → **Interim Analysis** → **Phase 2a (cont)**

14 patients



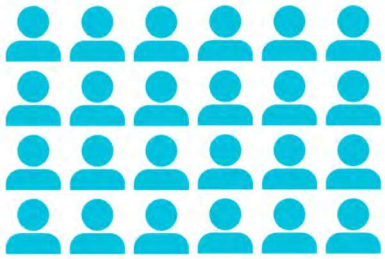
**COMPLETED**

26 patients



**RECRUITING**

24 patients



# ACCENT PHASE 1B SUMMARY

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

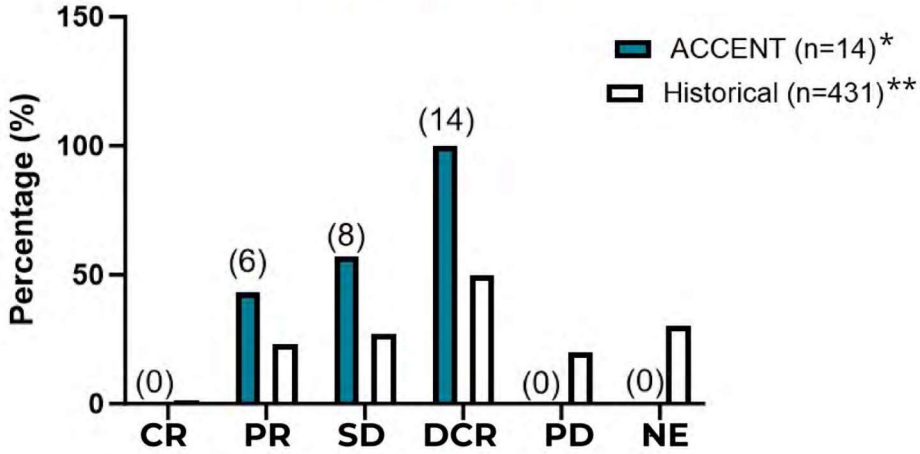
Safe and well tolerated

- 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

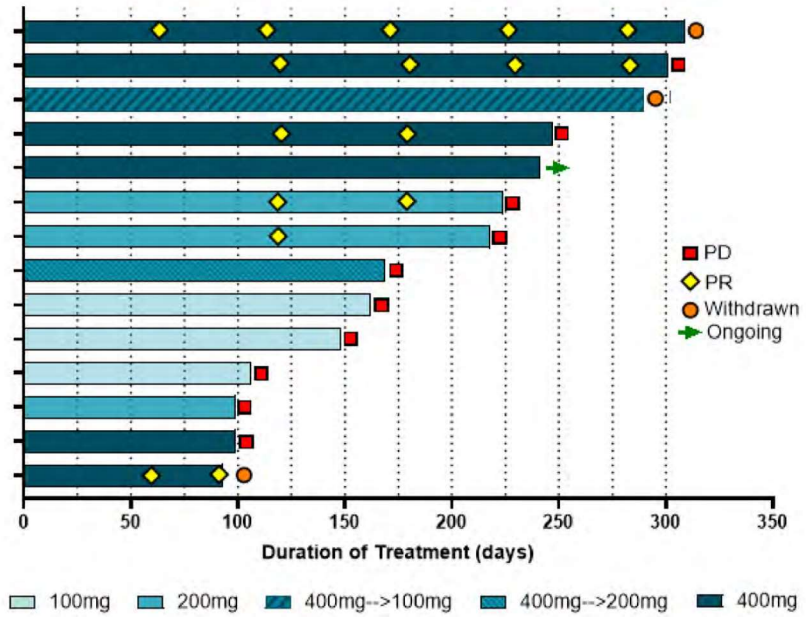
* Investigator reviewed

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

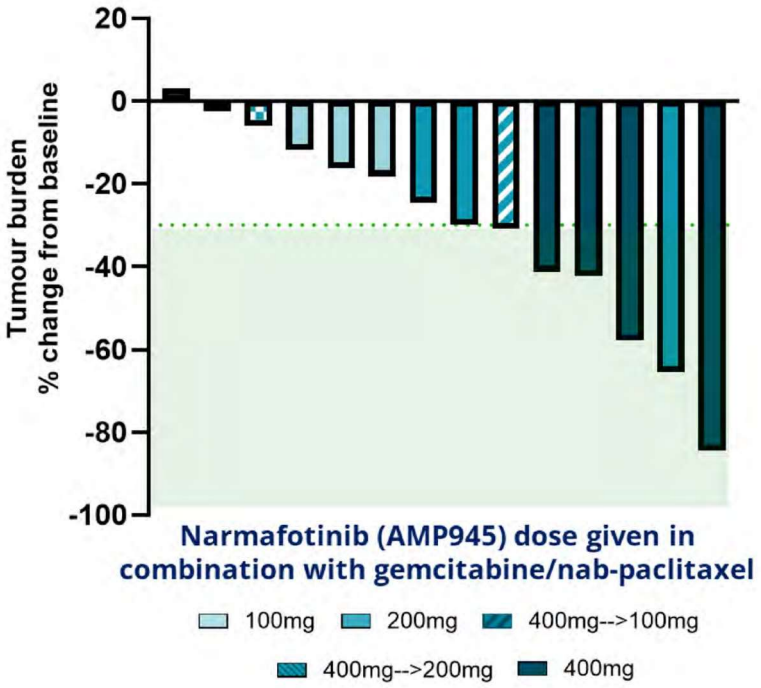
NB. Phase 1b trial not powered for efficacy

# 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

Amplia
THERAPEUTICS

**Chris Burns** PhD GAICD
CEO and MD

chris@ampliatx.com

Amplia Therapeutics Limited
ABN 16 165160 841
ASX: ATX
info@ampliatx.com

**ampliatx.com | @ampliatx**