ABN 16 165 160 841

ASX RELEASE **29th September 2023**

AACR PANCREATIC CANCER CONFERENCE PRESENTATION

HIGHLIGHTS

- *Preclinical data from pancreatic cancer studies presented at premier international conference in Boston, USA.*
- *Data from these studies further support combination of narmafotinib (AMP945) with chemotherapy in pancreatic cancer.*
- *Plans are underway for a clinical trial of narmafotinib in combination with FOLFIRINOX.*

Melbourne, Australia: Amplia Therapeutics Limited (ASX: ATX), ("Amplia" or the "Company") is pleased to announce that a poster, detailing a series of preclinical studies in pancreatic cancer models, was presented overnight at the **AACR SPECIAL CONFERENCE IN CANCER RESEARCH: PANCREATIC CANCER** meeting, being held in Boston, USA. The poster describes work conducted by our collaborators at the Garvan Institute of Medical Research, Sydney, and was presented by postdoctoral researcher Dr Kendelle Murphy.

A copy of the presentation is attached to this announcement.

Amplia's CEO Dr Chris Burns commented: "We are delighted that this extensive body of research from the Garvan Institute on our best-in-class FAK inhibitor narmafotinib is being presented at such a prestigious conference. The Garvan team have done an outstanding job and this poster represents the first public disclosure of the breadth of that work demonstrating the impressive activity of the drug in these preclinical studies."

The poster shows data demonstrating that in disease-bearing mice narmafotinib (AMP945) significantly reduces pancreatic cancer associated fibrosis through inhibition of FAK activity. Further, in a number of in vivo pancreatic cancer models, narmafotinib can be utilized to improve chemotherapy response.

Dr Burns continued: "This new preclinical data provides additional support for the activity of narmafotinib in combination with the two major chemotherapy regimens for pancreatic cancer. Plans are underway to start clinical trials using narmafotinib in combination with FOLFIRINOX in a similar design to the ACCENT trial."

This ASX announcement was approved and authorised for release by the Board.

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

Pulsed priming with narmafotinib reduces fibrosis and enhances both gemcitabine/Abraxane & FOLFIRINOX response in pancreatic cancer

Garvan Institute of Medical Research

Kendelle J Murphy*‡, Cecilia R Chambers†, Daniel A Reed†, Lily M Channon, Victoria Lee, Anna E Howell, Max Nobis, Astrid Magenau, Janett Stoehr, Brooke A Pereira, Sophie McKay, Anaiis Zaratzian, Michael Tayao, Andrew Da Silva, Australian Pancreatic Genome Initiative (APGI), Australian Pancreatic Matrix Atlas (APMA), Ruth J Lyons, Anthony J Gill, Andrew V Biankin, Jaswinder Samra, C Elizabeth Caldon, Thomas R Jeffry Evans, Lorraine Chantrill, Lisa G Horvath, Owen J Sansom, Jennifer P Morton, Tri G Phan, Yingxiao Wang, Terrie-Anne Cock, Anthony Bishop, Mark Devlin, John Lambert, Christopher J Burns, Thomas R Cox, Marina Pajic, David Herrmann*‡ and Paul Timpson*‡

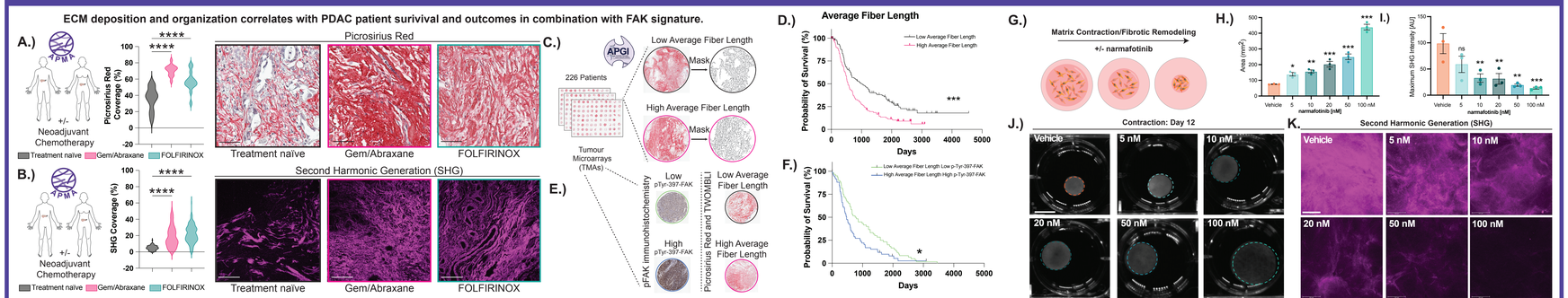
Amplia THERAPEUTICS

Introduction

- Pancreatic ductal adenocarcinoma (PDAC) is a highly fibrotic and aggressive malignancy with a poor 5-year survival rate of 12%.
- The standard-of-care for these patients is largely limited to one of two systemic chemotherapy regimens: Gemcitabine in combination with Abraxane (nab-paclitaxel) or FOLFIRINOX regimen consisting of oxaliplatin, irinotecan, leucovorin and 5-fluorouracil.
- PDAC progression is accompanied by a fibrotic response in the stroma, involving the elevated deposition and remodeling of extracellular matrix (ECM), promoting tissue stiffness and driving tumor progression as well as poor chemotherapeutic response.
- Focal Adhesion Kinase (FAK) is a non-receptor tyrosine kinase that modulates bidirectional interactions between cancer cells and their adjacent ECM via integrin-mediated signaling.
- We and others have recently shown that FAK inhibition can reduce fibrosis, supporting the clinical assessment of FAK inhibition for cancer treatment.

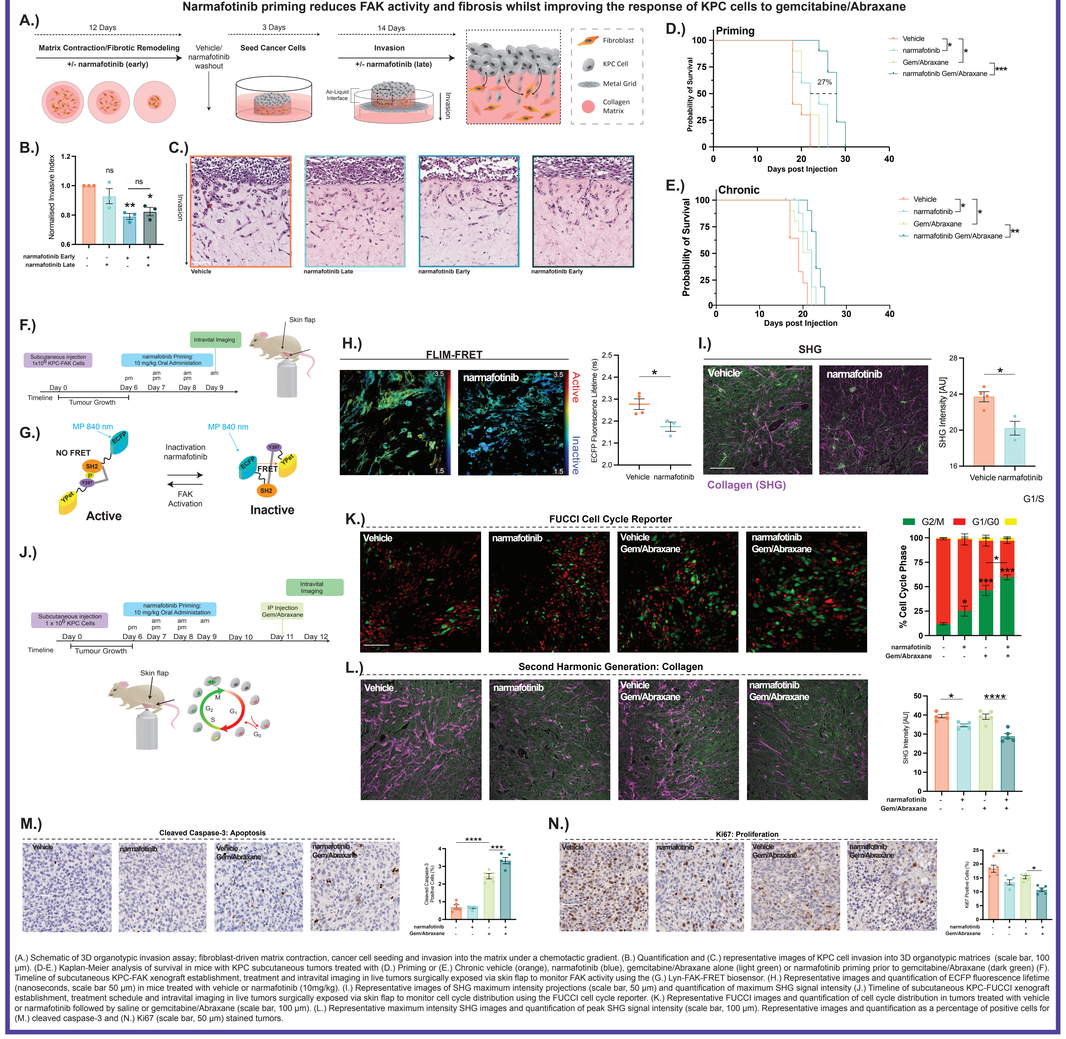
Here, we provide preclinical data showing that the ATP-competitive, orally bioavailable small molecule, narmafotinib; a highly potent and selective inhibitor of FAK, with desirable potency, selectivity, and pharmacokinetics (PK) in healthy human volunteers, which can be utilized to improve chemotherapy response in pancreatic cancer.

Fibrotic Targeting in PDAC



(A.) Quantification, and representative images of Picrosirius Red (B.) SHGimaging of tissues from PDAC patients (C.) Schematic representation of patient TMA establishment and staining with Picrosirius Red. (D.) Kaplan-Meier analysis of human PDAC survival based on average collagen fiber length (E.) Schematic representation of patient TMA staining with pTyr-397-FAK and Picrosirius Red. (F.) Kaplan-Meier analysis of human PDAC survival (G.) Schematic of 3D organotypic contraction assay. (H.) Quantification of matrix contraction at day 12 and (I.) SHG maximum intensity of contracted matrices at day 12. (J.) Representative images of matrix contraction (scale, 1 cm), and (K.) SHG maximum intensity (scale, 100 µm), at day 12.

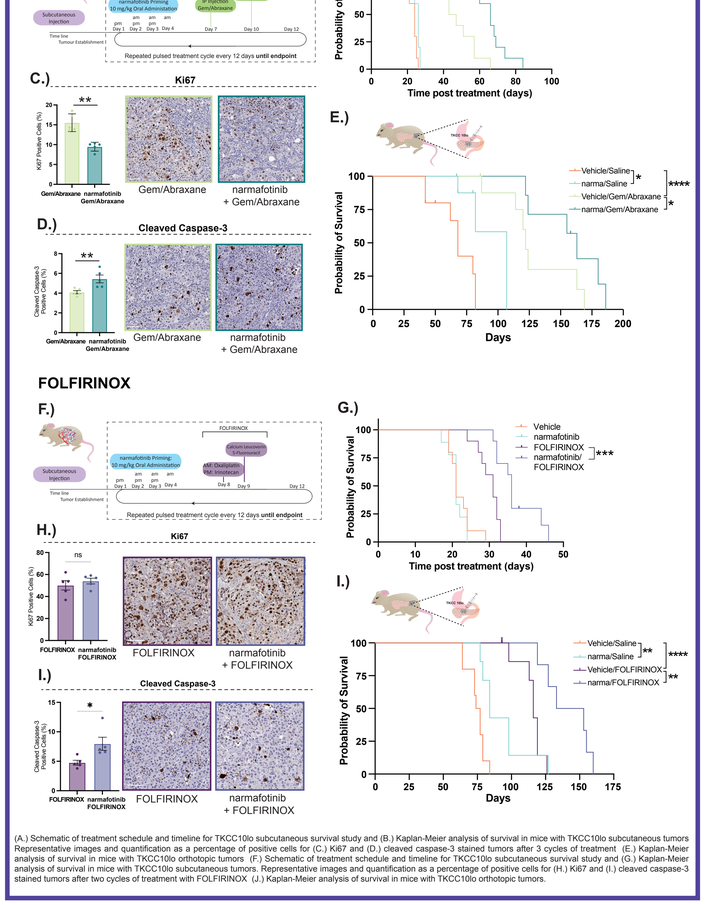
Pulsed Priming



(A.) Schematic of 3D organotypic invasion assay; fibroblast-driven matrix contraction, cancer cell seeding and invasion into the matrix under a chemotactic gradient. (B.) Quantification and (C.) representative images of KPC cell invasion into 3D organotypic matrices (scale bar, 100 µm). (D-E.) Kaplan-Meier analysis of survival in mice with KPC subcutaneous tumors treated with (D.) Priming or (E.) Chronic vehicle (orange), narmafotinib (blue), gemcitabine/Abraxane alone (light green) or narmafotinib priming prior to gemcitabine/Abraxane (dark green) (F). Timeline of subcutaneous KPC-FAK xenograft establishment, treatment and intravital imaging in live tumors surgically exposed via skin flap to monitor FAK activity using the (G.) Lyn-FAK-FRET biosensor. (H.) Representative images and quantification of ECFP fluorescence lifetime (nanoseconds, scale bar 50 µm) in mice treated with vehicle or narmafotinib (10mg/kg). (I.) Representative images of SHG maximum intensity projections (scale bar, 50 µm) and quantification of maximum SHG signal intensity (J.) Timeline of subcutaneous KPC-FUCCI xenograft establishment, treatment schedule and intravital imaging in live tumors surgically exposed via skin flap to monitor cell cycle distribution using the FUCCI cell cycle reporter. (K.) Representative FUCCI images and quantification of cell cycle distribution in tumors treated with vehicle or narmafotinib followed by saline or gemcitabine/Abraxane (scale bar, 100 µm). (L.) Representative maximum intensity SHG images and quantification of peak SHG signal intensity (scale bar, 100 µm). Representative images and quantification as a percentage of positive cells for (M.) cleaved caspase-3 and (N.) Ki67 (scale bar, 50 µm) stained tumors.

Personalised Medicine

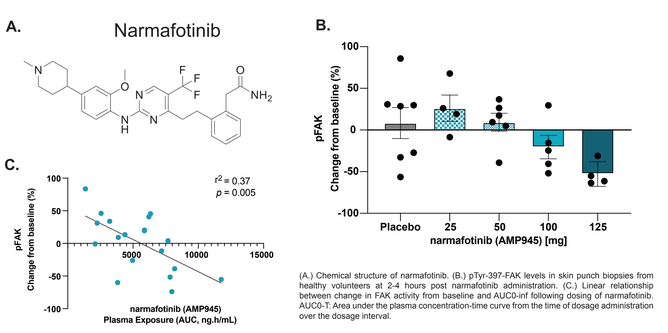
Narmafotinib priming prior to gemcitabine/Abraxane or FOLFIRINOX chemotherapy significantly extends survival in long-term orthotopic studies using patient-derived models.



(A.) Schematic of treatment schedule and timeline for TKCC10lo subcutaneous survival study and (B.) Kaplan-Meier analysis of survival in mice with TKCC10lo subcutaneous tumors Representative images and quantification as a percentage of positive cells for (C.) Ki67 and (D.) cleaved caspase-3 stained tumors after 3 cycles of treatment (E.) Kaplan-Meier analysis of survival in mice with TKCC10lo orthotopic tumors (F.) Schematic of treatment schedule and timeline for TKCC10lo subcutaneous survival study and (G.) Kaplan-Meier analysis of survival in mice with TKCC10lo subcutaneous tumors. Representative images and quantification as a percentage of positive cells for (H.) Ki67 and (I.) cleaved caspase-3 stained tumors after two cycles of treatment with FOLFIRINOX (J.) Kaplan-Meier analysis of survival in mice with TKCC10lo orthotopic tumors.

Clinical Translation: ACCENT Trial

- Narmafotinib (Amplia Therapeutics Ltd) was discovered through a structure-guided drug discovery program.
- ATP competitive small molecule inhibitor of FAK with a potency for FAK (IC_{50} 2.2nM) and is selective over the closely related kinase Pyk2 (IC50 550nM).
- Narmafotinib displays high selectivity across a panel of 468 kinases, along with favourable pharmacokinetics in murine species.
- In mice, orally dosed narmafotinib possesses a half-life of ~3 hours and oral bioavailability of 47%.
- A Phase I randomized double-blind, placebo-controlled study in 56 healthy volunteers was undertaken (ACTRN12620000894998) to investigate safety, tolerability, Pharmacokinetic and Pharmacodynamic effects of orally dosed drug.
- The single ascending dose study showed that narmafotinib could be detected in the plasma over 24 hours following administration at various dosages as low as 15 mg up to 125 mg.
- Dose and exposure-response in skin punch biopsies following a single treatment with narmafotinib showed drug target engagement through reduction of pTyr-397-FAK levels, with a clear dose demonstrated by a significant linear relationship between change in FAK activity from baseline.
- No serious or severe treatment emergent adverse events (TEAE)s, nor any TEAEs leading to study withdrawal were observed and the majority of TEAEs reported were mild.

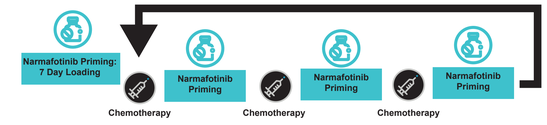


(A.) Chemical structure of narmafotinib. (B.) pTyr-397-FAK levels in skin punch biopsies from healthy volunteers at 2-4 hours post narmafotinib administration. (C.) Linear relationship between change in FAK activity from baseline and AUC0-inf following dosing of narmafotinib. AUC0-T: Area under the plasma concentration-time curve from the time of dosage administration over the dosage interval.

ACCENT Trial (NCT05355298)

-Pulsed dosing regimen of narmafotinib in combination with gemcitabine and Abraxane in first-line chemotherapy for patients with unresectable or metastatic pancreatic cancer.

-Patients will recieve one-week priming dosage of narmafotinib (once daily oral capsule). Gemcitabine and Abraxane will then be given according to standard-of care chemotherapy and patients given pulsed dosing of narmafotinib for four days prior to weekly chemotherapy.



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