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ASX RELEASE **20 January 2025**

NEW DATA FOR NARMAFOTINIB PRESENTED AT INTERNATIONAL CONFERENCE

HIGHLIGHTS

- *Additional data analysis from our Phase 1b/2a ACCENT trial in pancreatic cancer has been presented at the specialist scientific conference - the Keystone Meeting on the Tumour Microenvironment*
- *The data analysis further confirms the promising activity of narmafotinib at the 400 mg dose*
- *New preclinical data shows that narmafotinib enhances the activity of a drug that is used clinically to block the cancer-driving protein kRas in difficult-to-treat cancers, such as pancreatic cancer, lung cancer and colorectal cancer.*

Melbourne, Australia: Amplia Therapeutics Limited (ASX: ATX), ("Amplia" or the "Company") is pleased to announce that a poster, presenting new preclinical data and updated data from the ongoing ACCENT trial in pancreatic cancer, was presented overnight at prestigious Keystone meeting 'Tumor Microenvironment: Metastasis and the Host' in Banff, Canada. The ACCENT trial is the company's lead clinical program, exploring the activity of our best-in-class FAK inhibitor narmafotinib, in combination with standard-of-care chemotherapy, in advanced pancreatic cancer patients.

The poster describes preclinical data for narmafotinib in models of pancreatic cancer and presents further analysis of data from the Phase 1b portion of the ACCENT trial. Data highlights from the presentation include:

- Evidence from the ACCENT trial that there is a dose-dependent reduction in tumour size, as the oral dose of drug increases from 100 mg to 200 mg to 400 mg
- Data showing that patients on the 400 mg dose of narmafotinib had an average treatment duration of 8.3 months, significantly better than historical data for patients receiving chemotherapy alone
- Demonstration that narmafotinib has anti-fibrotic effects in a mouse model of pancreatic cancer and that narmafotinib has single-agent activity in this model
- Demonstration that narmafotinib enhances the activity of chemotherapy and appears to inhibit resistance to the chemotherapy that develops over time in the mouse model

In addition, the poster shows preliminary data demonstrating the beneficial effects of narmafotinib when combined with the approved drug adagrasib in mouse models of cancer. Adagrasib, marketed as Krazati®, inhibits a mutated form of the cancer causing protein kRas, which is present in a subset of pancreatic cancer patients as well as in patients with lung and colorectal cancer.

A copy of the poster is attached to this announcement.

Amplia's CEO Dr Chris Burns commented: "We are delighted to present further data about our drug narmafotinib and its activity in the ACCENT clinical trial. Demonstration of the drug's activity in cancer patients, as well as in defined animal models of cancer, helps to build a robust dataset that underpins the commercial potential of the drug."

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

About Narmafotinib

Narmafotinib (AMP945) is the company's best-in-class inhibitor of the protein FAK, a protein over-expressed in pancreatic and other cancers, and a drug target gaining increasing attention for its role in solid tumours. The drug, which is a highly potent and selective inhibitor of FAK, has shown promising data in a range of preclinical cancer studies. The drug has successfully completed a healthy volunteer study, and is currently in an open-label Phase 2a trial in pancreatic cancer where a combination of narmafotinib and the chemotherapies gemcitabine and Abraxane® is being assessed for safety, tolerability and efficacy.

About the ACCENT Trial

The ACCENT trial is entitled '*A Phase 1b/2a, Multicentre, Open Label Study of the Pharmacokinetics, Safety and Efficacy of AMP945 in Combination with Nab-paclitaxel and Gemcitabine in Pancreatic Cancer Patients*'.

The ACCENT trial explores the use of narmafotinib in combination with standard-of-care chemotherapy of gemcitabine and Abraxane® in first-line patients with advanced pancreatic cancer. The trial is a single-arm open label study conducted in two stages. The first stage (Phase 1b), completed in November 2023, identified a 400 mg oral daily dose of narmafotinib, given in the days preceding regular chemotherapy infusion, as safe and well tolerated.

The second stage (Phase 2a), of the trial is designed to assess drug efficacy in combination with gemcitabine and Abraxane. The primary endpoints are Objective Response Rate (ORR) and Duration on Trial (DOT) with secondary endpoints being Progression Free Survival (PFS) and Overall Survival (OS). Safety and tolerability will continue to be assessed.

More information about the ACCENT trial, including a list of participating sites can be found via the ACCENT website, the Amplia Therapeutics website, and at ClinicalTrials.gov under the identifier NCT05355298.

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 and ovarian 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) and LinkedIn.

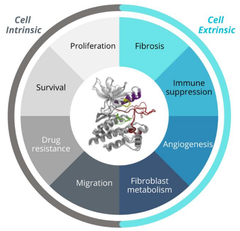
Focal Adhesion Kinase Inhibitor Narmafotinib Targets the Tumor and Microenvironment to Enhance and Sustain Sensitivity to Chemotherapy

Sarah Kinkel[1], Kendelle Murphy[2], David Herrmann[2], Paul Timpson[2], Nicole Kruger[1], Sumitra Ananda[3], Marion Harris[4], Lara Lipton[5], Adnan Nagrial[6], Nick Pavlakis[7], Jason Lickliter[1], Christopher J. Burns[1], Terrie-Anne Cock[1]

[1]Amplia Therapeutics, Melbourne, Australia; [2] Garvan Institute of Medical Research, Sydney, Australia; [3]Epworth Cancer Services Clinical Institute Melbourne, Australia; [4]Monash Medical Centre Melbourne, Australia; [5]Sunshine Hospital, Melbourne, Australia; [6]Westmead Cancer Care Centre, Sydney, Australia; [7]GenesisCare, Sydney, Australia.

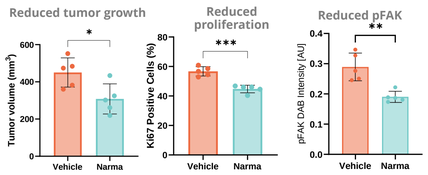
1. Narmafotinib (AMP945) is a selective and orally bioavailable inhibitor of Focal Adhesion Kinase (FAK)

- FAK is a non-receptor tyrosine kinase that acts through numerous signaling pathways to mediate communication between cells and their environment.
- FAK plays a crucial role in normal cellular stress response[1].
- Aberrant FAK signaling has been implicated in the progression of cancer, where it is involved in promoting tumor growth, adhesion, angiogenesis, invasion, and migration, as well as immunomodulation and remodeling of the fibrotic tumor microenvironment[2-4].
- FAK is frequently overexpressed in a variety of cancers, including pancreatic ductal adenocarcinoma[4], a highly fibrotic and aggressive malignancy with a poor 5-year survival rate[5], in which high FAK expression correlates with poor prognosis[6,7].

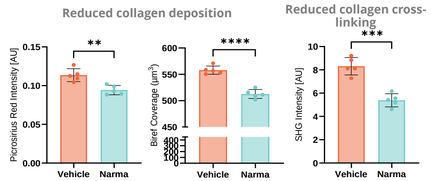


2. Narmafotinib treatment directly affects the tumor and microenvironment

Narmafotinib treatment reduced tumor growth & proliferation

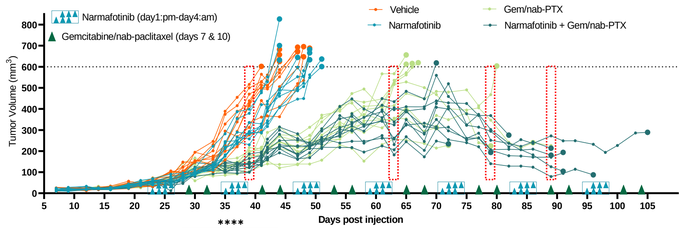


Narmafotinib treatment reduced tumor fibrosis

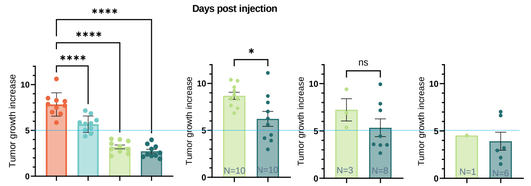


Mean ± SD; p-values determined using Welch's t test

3. Narmafotinib improves responsiveness to gemcitabine and nab-paclitaxel; tumors showed enhanced sensitivity to chemotherapy with sustained reduction in growth



90% of mice treated with a **narmafotinib combined with gemcitabine/ nab-paclitaxel** sustain sensitivity to chemotherapy

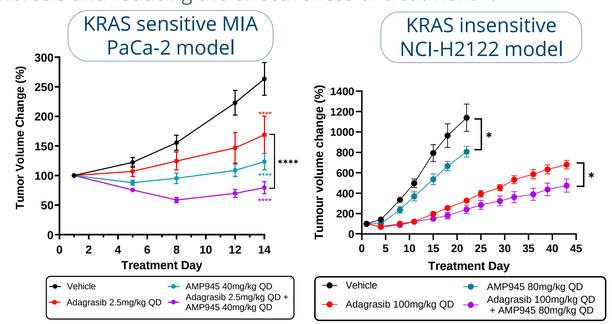


Mean ± SD; p-values determined using one-way ANOVA or Welch's t test.

Preclinical pancreatic cancer model: Patient-derived TKCC10lo cell line subcutaneous xenograft model treated with **vehicle**, **narmafotinib alone**, **gemcitabine/nab-paclitaxel** or **narmafotinib in combination with gemcitabine/nab-paclitaxel.**

5. Narmafotinib increases and sustains tumor responsiveness to KRAS G12C inhibitor adagrasib

KRAS mutations are common oncogenic drivers; KRAS G12C inhibition can hyperactivate FAK signaling, which can lead to fibrosis and reducing the effectiveness of treatment[10].



Mean ± SEM; p-values determined using 2-way ANOVA with Sidak's multiple comparison test (left panel) or unpaired t test (right panel).

Preclinical KRAS G12C mutant cancer model: MIA PaCa-2 (pancreatic) and NCI-H2122 (lung) subcutaneous xenograft model treated with **vehicle**, **narmafotinib alone**, **adagrasib alone** or **narmafotinib in combination with adagrasib.**

4. Clinical dose-dependent benefit of narmafotinib in combination with gemcitabine and nab-paclitaxel (Abraxane®) standard of care as first-line therapy in patients with metastatic pancreatic cancer: ACCENT trial (provisional analysis of Phase 1b)

The **ACCENT trial (NCT05355298)** is a Phase 1b/2a, open label study of the pharmacokinetics, safety and efficacy of narmafotinib in combination with gemcitabine and nab-paclitaxel (Abraxane®) standard of care (SOC), as first-line therapy in patients with advanced pancreatic cancer. The trial is a single-arm open-label study conducted in two stages.

*Dose selected for Phase 2

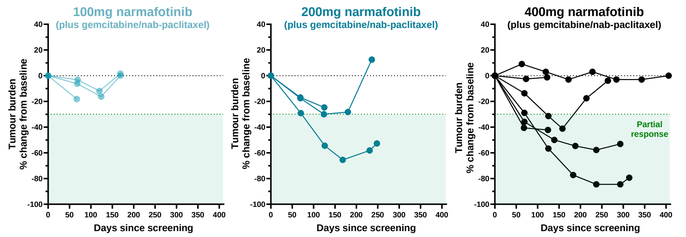
Part A (Phase 1b): patients with advanced pancreatic cancer were enrolled in a 3+3 design, with narmafotinib dose escalation (100, 200 and 400 mg), and the primary objective of determining recommended Phase 2 dose, and assessing safety and tolerability of oral narmafotinib administered prior to IV administration of gemcitabine and nab-paclitaxel.

Part B (Phase 2a) is a Simon's two-stage design, with the primary objectives of assessing safety, tolerability, and efficacy of the combination using RECIST v1.1.

- All participants received oral narmafotinib once daily at the selected dose on Day -8 to Day -2 (7 doses total) of a monotherapy run-in period, prior to first treatment cycle.
- Each 28-day treatment cycle includes IV gemcitabine and nab-paclitaxel on Days 1, 8 and 15, and oral narmafotinib priming on Days 3 to 6, 10 to 13, and 24 to 27, inclusive.

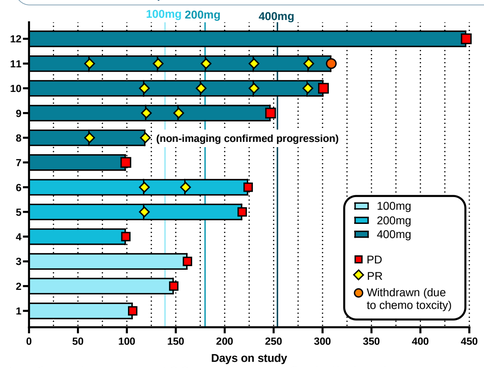
Dose-dependent reduction in tumor burden

- There were five confirmed partial responses (4 at 400 mg narmafotinib; 1 at 200 mg), indicating increased response with increasing dose.



Note: investigator read provisional analysis

Dose-dependent increase in treatment duration



Mean time on study for patients receiving **100mg**, **200mg** or **400mg** narmafotinib is indicated by bold lines on graph.

Note: Two dose-adjusted patients (400mg→100mg & 400mg→200mg) were included in safety and overall response analysis but are not shown on graphs.

- 6 patients on 400 mg narmafotinib had mean treatment duration of 8.3 months, with 4 of 6 patients on study for >6 months.
- Historical median duration of treatment for gemcitabine & nab-paclitaxel is 3.9 - 4.1 months; median time to treatment failure/duration of response is ~5 months[8,9].
- Narmafotinib in combination SOC was generally well-tolerated.

6. Conclusions

- Narmafotinib reduces tumor growth and fibrosis in a patient-derived pancreatic cancer xenograft model
- Narmafotinib enhances sensitivity to gemcitabine/nab-paclitaxel in preclinical models to sustain tumor growth reduction and increase overall survival
- Preclinical analysis indicates that narmafotinib shows efficacy in combination with KRAS G12C inhibitor adagrasib
- In the clinic (Phase 1b), narmafotinib combined with gemcitabine/nab-paclitaxel demonstrated promising activity in a dose-dependent manner in response and duration of treatment
  - Five confirmed partial responses (4 at 400 mg narmafotinib; 1 at 200 mg), indicating increased response with increasing dose
  - 400 mg of narmafotinib and gemcitabine/nab-paclitaxel mean duration of treatment was 8.3 months, out-performing historical SOC ~4 months
  - Narmafotinib in combination SOC was generally well-tolerated

Contact
Terrie-Anne Cock PhD
E: TerrieAnne@ampliatx.com
W: www.ampliatx.com

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** p < 0.05*
*** p < 0.01*
**** p < 0.001*
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