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ACCENT TRIAL DATA UPDATE PRESENTED AT INTERNATIONAL CONFERENCE

HIGHLIGHTS

- *Interim data from Amplia's ACCENT trial in pancreatic cancer is being presented at the prestigious American Association of Cancer Research (AACR) annual meeting*
- *The ACCENT trial investigates the combination of narmafotinib (AMP945) with standard-of-care chemotherapy*
- *The data presented highlights that narmafotinib is well tolerated in advanced pancreatic patients, with promising signs of activity substantially better than chemotherapy alone*

Melbourne, Australia: Amplia Therapeutics Limited (ASX: ATX), ("Amplia" or the "Company") is pleased to announce that a poster highlighting key data from the ongoing ACCENT trial is being presented today at the annual meeting of the AACR, being held in Chicago, USA. The ACCENT trial explores the activity of our best-in-class FAK inhibitor narmafotinib, in combination with standard-of-care chemotherapy, in advanced pancreatic cancer patients.

The poster presentation outlines the scientific rationale for the use of FAK inhibitors in pancreatic cancer treatment, describes the clinical design of the ACCENT trial, and presents a detailed analysis of data up to 7 March 2025 for the first 29 patients of the 55 enrolled in the trial.

Classification	Narmafotinib + Chemotherapy	Chemotherapy alone[#]
	Best Response % (n)	Best Overall response % (n)
No. of Patients	29	431
Complete Response (CR)	0% (0)	<1% (1)
Partial Response (PR)	38% (11)	23% (98)
Stable Disease (SD)	41% (12)	27% (118)
Disease Control Rate (DCR) (=CR+PR+SD)	79% (23)	50% (216)
Progressive Disease (PD)	10% (3)	20% (86)
Not Evaluable (NE)	10% (3)	30% (128)
Median Duration on Trial	208 days	117 days

Table: Interim data for ACCENT trial compared to chemotherapy alone ([#] data from *New England Journal of Medicine* 2013; 369: 1691 – 703).

Key highlights from the data presented include efficacy and duration-on-trial readouts for the narmafotinib + chemotherapy combination that are substantially better than the benchmark study of chemotherapy alone (see Table). Further, 21 patients recorded a reduction in tumour size with 15 of those showing a >30% tumour shrinkage. Of these patients, 11 recorded a sustained reduction in tumour size for >2 months (recorded as a confirmed partial response).

Safety and tolerability data, with a data cut-off of 3 February 2025, is also presented for 39 patients enrolled in the trial, continues to demonstrate that narmafotinib is well tolerated. The most common treatment emergent adverse events, which were typically assessed as related to the chemotherapy rather than narmafotinib, included nausea, diarrhoea, fatigue, and constipation. The most common narmafotinib-related treatment related adverse events were nausea, diarrhoea, and gastroesophageal reflux which were predominantly mild to moderate.

A copy of the poster, entitled *Narmafotinib (AMP945) in combination with gemcitabine and nab-paclitaxel in first-line patients with advanced pancreatic cancer (ACCENT trial) a Phase 1b/2a study: Interim analysis* is attached to this announcement.

Amplia CEO and MD Dr Chris Burns commented: "The combined data presented today at AACR continues to demonstrate the significant promise narmafotinib, in combination with chemotherapy, has in the treatment of advanced pancreatic cancer. We look forward to presenting more mature data in the coming months for the full cohort of 55 patients."

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 cancer 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 successfully completed a healthy volunteer study in 2021 and is currently being investigated in advanced pancreatic cancer in the ACCENT trial. The drug has Fast-Track and Orphan Drug Designation for pancreatic cancer from the US FDA. Plans for a US trial, under an open IND, in combination with FOLFIRINOX are well advanced.

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 trial is a single-arm open label study conducted in two stages. The first stage (Phase 1b), completed in November 2023, determined an optimal dose of narmafotinib (AMP945) by assessing the safety, tolerability, pharmacokinetics and preliminary efficacy when dosed in combination with gemcitabine and Abraxane in first-line patients with advanced pancreatic cancer.

The second stage (Phase 2a) of the trial is designed to assess 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. A total of 55 patients have been enrolled in the trial which is being conducted at seven sites in Australia and five sites in South Korea.

More information about the ACCENT trial can be found via the ACCENT trial site, the Amplia Therapeutics website and at ClinicalTrials.gov under the identifier NCT05355298.

The Company will provide further updates on the trial as data is accrued.

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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.

Narmafotinib (AMP945) in combination with gemcitabine and nab-paclitaxel (Abraxane®) in first-line patients with advanced pancreatic cancer (ACCENT trial) a Phase 1b/2a study: Part B interim analysis

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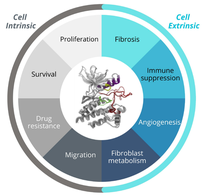
Narmafotinib

- 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 (PDAC)[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].

ACCENT Study Overview

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.

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.

Dosing regimen:

- 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.

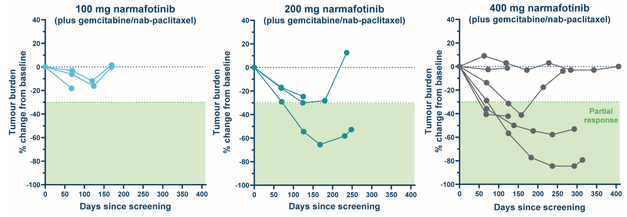
Key Eligibility Criteria:

Inclusion	Exclusion
• Diagnosis of metastatic PDAC (non-resectable local disease also allowed in Part A only) • ECOG status of 0 or 1 • Measurable disease per RECIST 1.1 • Life expectancy ≥ 3 months • Acceptable hematologic and clinical laboratory chemistry values	• Received prior treatment for metastatic disease • Unable to receive gemcitabine or nab-paclitaxel • Known brain metastases, unless treated and well-controlled for > 3 months • GI condition that could interfere with swallowing or absorption of medication

ACCENT Part A- Dose Escalation

In Part A, narmafotinib combined with gemcitabine and nab-paclitaxel demonstrated **promising activity in a dose-dependent manner in both 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, exceeding the historical SOC of ~4 months duration
- Narmafotinib in combination SOC was generally well-tolerated
- **400 mg narmafotinib dose selected for Part B**



ACCENT Part B- Encouraging Efficacy of Narmafotinib (400 mg) in combination with Gem/Nab-P

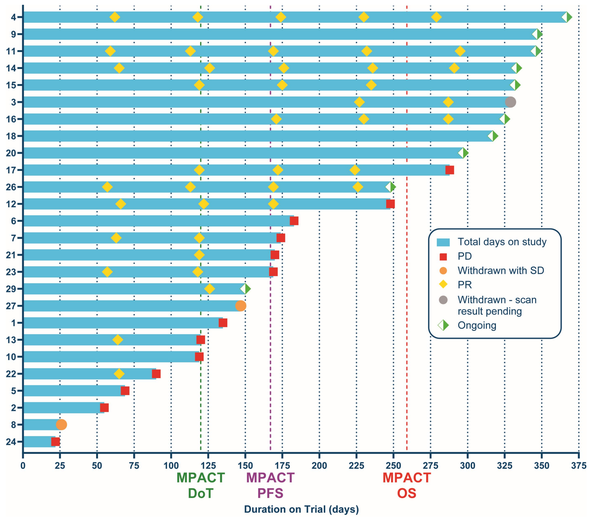
As of the cut-off date **7th March 2025**, all patients planned for the ACCENT Phase 2a study have been recruited in Australia and South Korea (55 patients in total).

The preliminary results presented here include safety data for 39 patients (cut off 3rd Feb 2025) and efficacy data for 29 patients (cut-off 7th March 2025), representing the first 26 evaluable patients (i.e. patients with post-baseline on-study scans);

Patient demographics for 29 patients evaluated for interim efficacy :

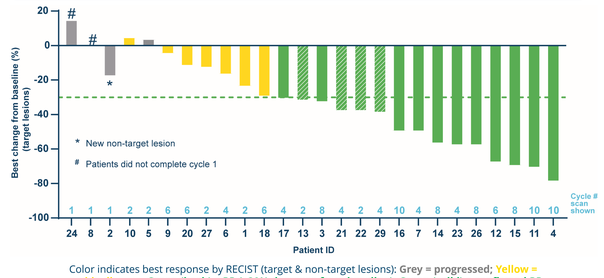
- Females: n = 15 (52%); males: n = 14 (48%)
- Median age, yrs (range): 63 (37 – 76)
- Race Caucasian n= 11 (40%); Asian n=18 (60%)
- 13 from Australia, 16 from South Korea

Duration on trial (DoT) for Narmafotinib (400 mg) in combination with Gem/Nab-P demonstrates a notable improvement over the historical data Gem/Nab-P alone



- **Duration on trial average ~7 months (208 days);** range: 22 – 367 days (10 patients are still on trial).
- 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 and PFS is 5.5 - 5.6 months[8,9].
- To date, 10/26 (38%) have already been on trial longer than the historical median OS of 8.5-9.2 months Gem/Nab-P [8,9].
- *Historical reference data is based on MPACT and NAPOLI 3 phase 3 trials with Gem/Nab-P in mPDAC patients[8,9].*

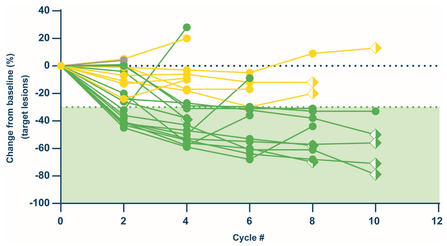
Encouraging Antitumor Activity



Color indicates best response by RECIST (target & non-target lesions): Grey = progressed; Yellow = stable disease; Green (hash) = PR (≥30% decrease from baseline); Green (solid) = confirmed PR

- 58% (15/26) of evaluable patients achieved a partial response (PR) and **11 PRs have been confirmed to date**

Early and Sustained Response: Target lesions change from baseline over time



Arrow indicates patients still on trial; only patients (n = 23) with a valid 8-week RECIST scan are shown

- A meaningful early reduction in tumor burden has been achieved in 9 patients after cycle 2 and 13 patients by cycle 4
- **Most patients had a sustained response for >6 months**; comprising of both PR and SD responses

Classification	Best Overall Response
(n)	29
CR	0 (0%)
Confirmed PR	11 (37.9%)
SD	12 (41.2%)
DCR (PR+SD)	23 (79.3%)
PD	3 (10.3%)
Not Evaluable	3 (10.3%)

- Of the 15 PRs, so far 11 have been confirmed in this ongoing study.
- Disease control rate (DCR) of 79.3% for narmafotinib (400 mg) in combination with Gem/Nab-P
- Substantial improvement over historical DCR for Gem/Nab-P alone of 48-62% [8,9]

Narmafotinib (400 mg) in Combination with Gem/Nab-P is Well Tolerated in mPDAC Patients

Summary of Frequently Reported Treatment Emergent Adverse Event (TEAEs) Part B (≥ 10% Participants)

Adverse Event	TEAE PART B (N=39)^ n (%) E
Participants with at least one TEAE	39 (100) 541
Neuropathy peripheral	14 (35.9) 20
Nausea	13 (33.3) 21
Diarrhea	12 (30.8) 20
Fatigue	12 (30.8) 15
Neutrophil count decreased	11 (28.2) 36
Constipation	11 (28.2) 13
Anemia	9 (23.1) 17
Pyrexia	9 (23.1) 14
Decreased appetite	9 (23.1) 12
Vomiting	8 (20.5) 10
Rash	8 (20.5) 10
Abdominal pain	7 (17.9) 13
Stomatitis	6 (15.4) 8
Gastroesophageal reflux	6 (15.4) 7
Insomnia	5 (12.8) 6
Edema peripheral	5 (12.8) 5
Hypokalemia	5 (12.8) 5
Dyspnoea	5 (12.8) 5
Epistaxis	5 (12.8) 5
Back pain	4 (10.3) 7
Neutropenia	4 (10.3) 6
Edema	4 (10.3) 4
Peripheral sensory neuropathy	4 (10.3) 4
Alopecia	4 (10.3) 4

Most common TEAEs of any grade: peripheral neuropathy, nausea, diarrhea, fatigue, constipation, and decreased neutrophil count.

Grade 3 and 4 TEAEs: Of these, ≥2 participants: decreased neutrophil count, pyrexia, anemia, abdominal pain, neutropenia, nausea, cholangitis, cellulitis, and Clostridium difficile colitis.

These events were typically assessed as related to gemcitabine and/or nab-paclitaxel rather than narmafotinib.

There were no treatment related deaths.

Summary of Narmafotinib 400 mg Treatment Related Adverse Events (TRAEs) Part B (≥ 5% Participants)

Adverse event	TRAEs Narmafotinib 400 mg (N=39)^ n (%) E
Constipation	2 (5.1) 2
Diarrhea	5 (12.8) 7
Dyspepsia	2 (5.1) 3
Gastroesophageal reflux	4 (10.3) 5
Nausea	8 (20.5) 12
Vomiting	2 (5.1) 2

^55 participants have been enrolled to this cohort, but AE data is currently only available for 39 participants (cut off 03 February 2025). Participants who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Abbreviations; E = number of adverse events; N, n = number of participants; TEAE = treatment emergent adverse event; TRAE = treatment related adverse event.

- **The most common narmafotinib-related TRAEs in Part B were gastrointestinal events: nausea, diarrhea, and gastroesophageal reflux which were predominantly mild to moderate**
- Narmafotinib related severe events (n=3), each occurring on one occasion: abdominal pain, nausea, and one uncoded event
- SAEs assessed as possibly related to narmafotinib: nausea (n=1), vomiting (n=2)

Conclusion

- **Preliminary Part B analysis showed narmafotinib (400 mg) in combination with Gem/Nab-P to be well-tolerated with promising signs of efficacy**.
- The compelling narmafotinib profile supports multiple potential combination development strategies. Thus, Amplia is initiating (Q2 2025) a **Phase 1b/2a study to investigate narmafotinib in combination with modified FOLFIRINOX in pancreatic cancer patients (AMP945-PC-202)**

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