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AACR CONFERENCE PRESENTATION

HIGHLIGHTS

- *Data from our Phase 1b ACCENT trial in pancreatic cancer has been presented at the prestigious American Association of Cancer Research annual meeting*
- *The data summary highlights that narmafotinib in advanced pancreatic patients appears safe and well tolerated, with promising early signs of activity*

Melbourne, Australia: Amplia Therapeutics Limited (ASX: ATX), ("Amplia" or the "Company") is pleased to announce that a poster, highlighting key data from the Phase 1b ACCENT trial, was presented overnight at the annual meeting of the American Association of Cancer Research, being held in San Diego, USA. 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 outlines the scientific rationale for the use of FAK inhibitors in pancreatic cancer treatment and details the clinical design of the ACCENT trial. Data highlights from the presented data for the 14 patients in the Phase 1b trial include:

- Demonstration of the excellent pharmacokinetics of the drug in patients, supporting once-a-day daily dosing
- Excellent safety and tolerability data
- Response data showing a disease control rate, as best response, of 100% (= 6 partial responses and 8 stable disease)
- Evidence that the higher doses of 200 and 400 mg resulted in better outcomes
- Promising duration on trial showing 9 of 14 patients stayed on trial for >5 months.

A copy of the poster is attached to this announcement.

Amplia's CEO Dr Chris Burns commented: "We are delighted to present this early data from the ACCENT trial to the broader scientific and clinical community at such a high profile conference. Such disclosures allow us to discuss the data with world-leading experts in FAK biology and oncology drug development, as well as potential collaboration partners in pharma and biotech."

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.

Phase 1b/2a of narmafotinib (AMP945) in combination with gemcitabine and nab-paclitaxel (Abraxane®) standard of care as first-line therapy in patients with advanced pancreatic cancer (ACCENT trial): interim analysis

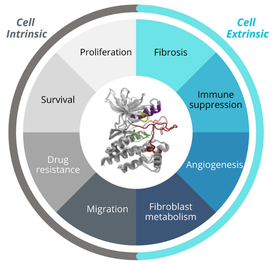
Terrie-Anne Cock[1], Anthony Bishop[1], Nicole Kruger[1], Sarah McCormack[1], Marion Harris[2], Sumitra Ananda[3], Lara Lipton[4], Adnan Nagrial[5], Nick Pavlakis[6], Warren Joubert[7], Laura Donato[8], Jason D. Lickliter[1], Christopher J. Burns[1]

[1]Amplia Therapeutics, Melbourne, Australia, [2]Monash Medical Centre, Melbourne, Australia, [3]Epworth Cancer Services Clinical Institute, Melbourne, Australia, [4]Sunshine Hospital, Melbourne, Australia, [5]Westmead Cancer Care Centre, Sydney Australia, [6]GenesisCare, Sydney Australia, [7]Greenslopes Oncology, Brisbane, Australia and [8] IQVIA Biotech, Sydney, Australia

Background

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 key signaling pathways to mediate communication between cells and their environment and plays a crucial role in normal cellular stress response, acting to buffer healthy cells from dying when exposed to extreme cellular stress[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

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 as first-line therapy in patients with advanced pancreatic cancer. The trial is a single-arm open label study conducted in two stages.

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

14 patients – dose escalation:
Cohort 1 - 100mg (n=3)
Cohort 2 - 200mg (n=3)
Cohort 3 - 400mg (n=8)

RP2D = 400mg

26 patients

24 patients

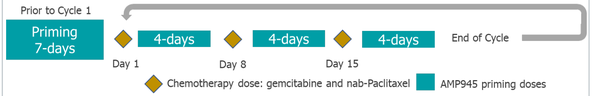
RECRUITING

COMPLETED

Part A (Phase 1b), patients were enrolled in a 3+3 design to determine the narmafotinib recommended Phase 2 dose (RP2D), with dose-escalation (100, 200 and 400 mg), with a primary objective of determining recommended RP2D, and assessing safety and tolerability of oral narmafotinib administered prior to IV administration of gemcitabine and nab-paclitaxel in participants with advanced pancreatic cancer.

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 (central read by indep't reviewers).

Dosing Regimens



All participants receive 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 the first treatment cycle. Each 28-day treatment cycle includes IV nab-paclitaxel (Abraxane®) and gemcitabine 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 or not surgically resectable PDAC • 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 systemic treatment for PDAC, except as a radiosensitizer, provided >6 months have elapsed since last dose and no toxicities >grade 1 are still present • Known brain metastases, unless treated and well-controlled for > 3 months • GI condition that could interfere with swallowing or absorption of medication

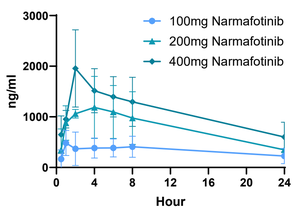
Patient demographics: Part A dose escalation

14 patients were treated with narmafotinib + gemcitabine/nab-paclitaxel (Abraxane®)

- Males n=7 (50%)
- Females n=7 (50%)
- Average age: 62 years old
- Predominantly Caucasian

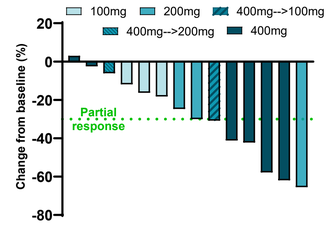
Pharmacokinetics

- Narmafotinib plasma PK samples were collected on Days -8, -7, 1, 3, 8, and 10 of Run-In/Cycle 1
- The PK for narmafotinib is dose-proportional across the dose range tested, and the half-life supports once a day dosing
- The chemotherapy regimen used in this study did not impact narmafotinib PK



Pharmacokinetics from single dose of narmafotinib (Day -8)

Best Response by RECIST v 1.1

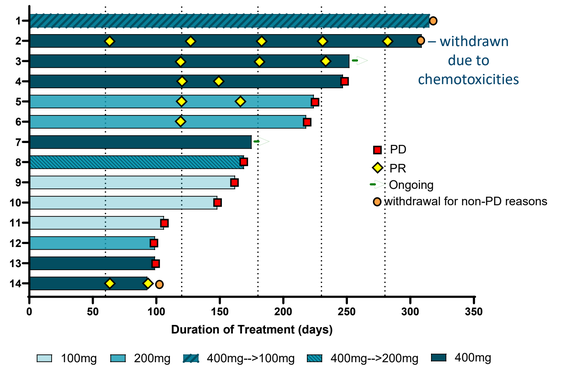


Classification	Best Overall Response
(n)	14
CR	0 (0%)
PR	6 (43%)
SD	8 (57%)
DCR (PR+SD)	14 (100%)
PD	0 (0%)
Not Evaluable	0 (0%)

Investigator assessed

- Narmafotinib combined with gemcitabine/nab-paclitaxel (Abraxane®) demonstrated promising dose related trend in the first 14 patients – with ORR of 43%.
- This compares favorably with the reported response rate of 23% with gemcitabine/Abraxane® in the pivotal Phase III trial[8].
- Two patients had dose adjustments due to AEs from 400mg to 100mg and 400mg to 200mg

Time on treatment



- All patients who completed their first 28-day cycle of treatment elected to stay on narmafotinib
- 9 of 14 patients on drug > 5 months
- There was a dose dependent trend in duration of treatment with the highest dose of narmafotinib (400 mg QD) associated with the longest duration of treatment, 212 days (mean duration)

Safety

- Narmafotinib-related events - the following occurred in more than one participant: diarrhea, gastroesophageal reflux disease, nausea, vomiting, fatigue, pyrexia, and macro-papular rash
- No treatment related deaths and only two narmafotinib related SAEs: febrile infection, and fatigue
- All other SAEs reported to date have either been unrelated or assessed as related to gemcitabine/Abraxane®
- No dose limiting toxicities (DLTs) were noted in the 100 mg and 200 mg cohorts. A single DLT (Grade 3 Nausea >72 h) was reported at the 400 mg dose
- Two patients had dose adjustments due to AEs from 400mg to 100mg and 400mg to 200mg
- No MTD was defined for narmafotinib

		Grade 3 or above					
		Related			Unrelated		
System Organ Class	Preferred Term	Narma-fotinib (N=15)	Gemci-tabine (N=14)	Nab-Paclitaxel (N=14)	Any Related	Not Related	All Events
		n (%) E					
Blood and lymphatic system disorders	Anaemia	0	1 (7) 1	1 (7) 1	1 (7) 1	0	1 (7) 1
Gastrointestinal disorders	Nausea	1 (7) 1	1 (7) 1	1 (7) 1	1 (7) 1	0	1 (7) 1
	Vomiting	1 (7) 1	1 (7) 1	1 (7) 1	1 (7) 1	0	1 (7) 1
General disorders & administration site conditions	Fatigue	1 (7) 1	1 (7) 1	1 (7) 1	1 (7) 1	0	1 (7) 1
	Febrile infection	1 (7) 1	0	0	1 (7) 1	0	1 (7) 1
	Pyrexia	0	2 (13) 3	2 (13) 3	2 (13) 3	2 (13) 2	3 (20) 5
Injury, poisoning & procedural complications	Toxicity to various agents	0	1 (7) 1	1 (7) 1	1 (7) 1	0	1 (7) 1
Metabolism & nutrition disorders	Dehydration	0	1 (7) 1	1 (7) 1	1 (7) 1	0	1 (7) 1

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). Percentage (%) of participants (n) are calculated based on the number of participants for the respective dose level (N).

Conclusions

- ✓ Dose escalation assessed 100 mg, 200 mg, 400 mg once daily
- ✓ Excellent once a day, dose proportional pharmacokinetics
- ✓ Safe and well tolerated
- ✓ Narmafotinib combined with gemcitabine/nab-paclitaxel (Abraxane®) demonstrates promising activity, with investigator assessed response rate of 43%
- ✓ Based on this promising Phase 1b data, 400 mg of narmafotinib has been selected for RP2D and the trial will proceed through Simon's Two Stage design and enroll up to 50 patients as part of the Phase 2 expansion cohort

Contact

Terrie-Anne Cock
Amplia Therapeutics
Email: TerrieAnne@ampliatx.com
Website: www.ampliatx.com

TUMOR MICROENVIROMENT WORKING GROUP
AACR American Association for Cancer Research

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