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LORNE CANCER CONFERENCE PRESENTATION

- *ACCENT clinical trial presented at premier national cancer conference in Lorne, Victoria.*

Melbourne, Australia: Amplia Therapeutics Limited (ASX: ATX), ("Amplia" or the "Company"), a company developing new approaches for the treatment of cancer and fibrosis, is pleased to announce that it has today presented the design and rationale for its ACCENT clinical trial at the **35th Annual Lorne Cancer Conference**, being held in Lorne, Victoria. The trial is currently underway and is recruiting patients at seven Australian sites.

A copy of the presentation is attached to this announcement.

Amplia's CEO Dr Chris Burns commented that "We are delighted to present our work at Australia's premier cancer conference which is attended by cancer researchers and oncologists from around Australia and the world. The poster describes the scientific rationale and preclinical data behind the novel pulsed dosing approach being employed in the ACCENT pancreatic cancer trial with our FAK inhibitor AMP945."

In addition to the poster presentation, Amplia Therapeutics' academic collaborator Dr Kendelle Murphy of the Garvan Institute, Sydney, is presenting a lecture in the opening session of the conference entitled '*Intravital imaging technology guides FAK-mediated priming in pancreatic cancer precision medicine*' detailing the value of FAK inhibition in preclinical models of pancreatic cancer.

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

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

A novel Focal Adhesion Kinase inhibitor AMP945 for first-line treatment of pancreatic cancer

Authors

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Overview

Amplia Introduction

Amplia Therapeutics Limited (ASX: ATX, Amplia) is a clinical-stage drug development company focused on the development of potent, orally available inhibitors of Focal Adhesion Kinase (FAK) for the treatment of cancer and fibrotic diseases.
Amplia's pipeline drugs were originally developed by the Cancer Therapeutics Cooperative Research Centre. Amplia was established to advance these promising drugs into clinical development and commercialisation.

FAK in Pancreatic Cancer

- FAK is a nonreceptor protein tyrosine kinase that is primarily regulated by integrin signalling.
- FAK controls fundamental cellular processes such as cell adhesion, migration, proliferation, and survival, and promotes important malignant features in cancer progression including tumour angiogenesis, chemotherapeutic resistance, and fibrosis in the stroma.
- FAK expression is frequently upregulated in different types of cancer and contributes to cancer progression by regulating the tumour microenvironment. Several FAK inhibitors are currently in early clinical development.

AMP 945 Overview

- AMP945 is a small molecule, selective and orally bioavailable inhibitor of FAK. FAK plays a key role in tumor cell growth, particularly immunosuppression, cancer cell invasion and metastasis and also contributes to multiple mechanisms underlying fibrosis.
- FAK has been associated with the activity of myofibroblasts and collagen deposition and remodelling in pancreatic cancer. Accordingly, FAK inhibitors offer promising new clinical opportunities for improving patient survival in both pancreatic cancer and other fibrotic cancer types.
- In preclinical studies, AMP945 displays potent anti-fibrotic activity in vitro and in vivo.
- In mouse models of pancreatic cancer, pulsed dosing of AMP945 added to gemcitabine/nab-paclitaxel inhibited collagen deposition and cross-linking and potentiated the effect of chemotherapy leading to increased survival.

Pre-clinical Evidence

Anti-FAK Activity

FAK has been associated with the activity of myofibroblasts and collagen deposition and remodelling in pancreatic cancer. In preclinical studies.

Using immunohistochemistry it was shown that AMP945 treatment led to significantly decreased levels of p-FAK in the tumour compared to vehicle treated mice (Figure 1). Tumour cells derived from the mouse pancreatic tumour line KPC were implanted subcutaneously into the flanks of Balb/c nude mice. Once tumours became palpable, mice were randomised to receive oral vehicle or AMP945 10 mg/kg BID for 3 days.

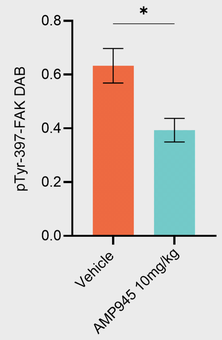


Figure 1 AMP945 leads to reduction in p-FAK in tumour

AMP945 Increased Survival

Mice were implanted with patient derived pancreatic cancer cells (TKCC) and held until the tumour was palpable. The mice were dosed with AMP945 on Day 1-4 and treated with gemcitabine and nab-paclitaxel on Day 7 and Day 10. This cycle was repeated every 12 days until the experimental endpoint was reached. Median survival times for mice receiving AMP945, gemcitabine and nab-paclitaxel were longer than those receiving only gemcitabine and nab-paclitaxel.

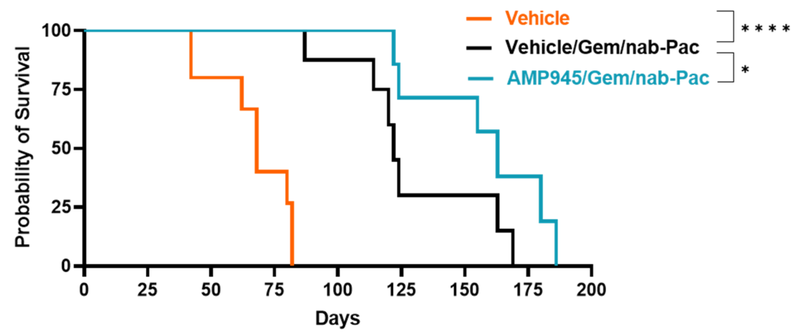


Figure 2: PDX model shows AMP945 boosts efficacy of gemcitabine and nab-paclitaxel

Pulsed Dosing Increases Survival

Mice were implanted with ectopic KPC pancreatic cancers and were treated with gemcitabine and nab-paclitaxel and either twice daily (chronic) of AMP945 (Figure 3) or pulsed doses of AMP945 (Figure 4). After an ethical endpoint their tumors were harvested. Median survival times for mice receiving pulsed doses of AMP945 were longer than those receiving daily doses.

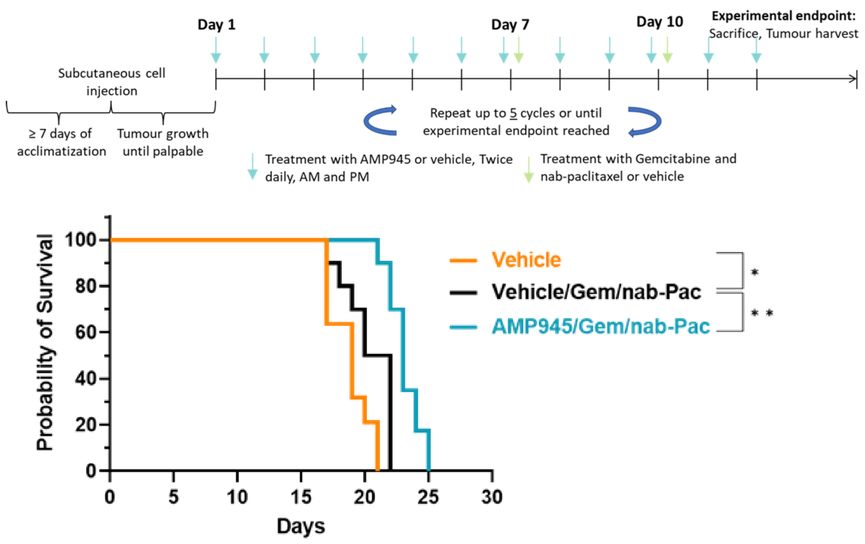


Figure 3: Dosing schedule and Kaplan-Meier survival for KPC tumour-bearing mice treated with vehicle, chronic AMP945, gemcitabine and nab-paclitaxel

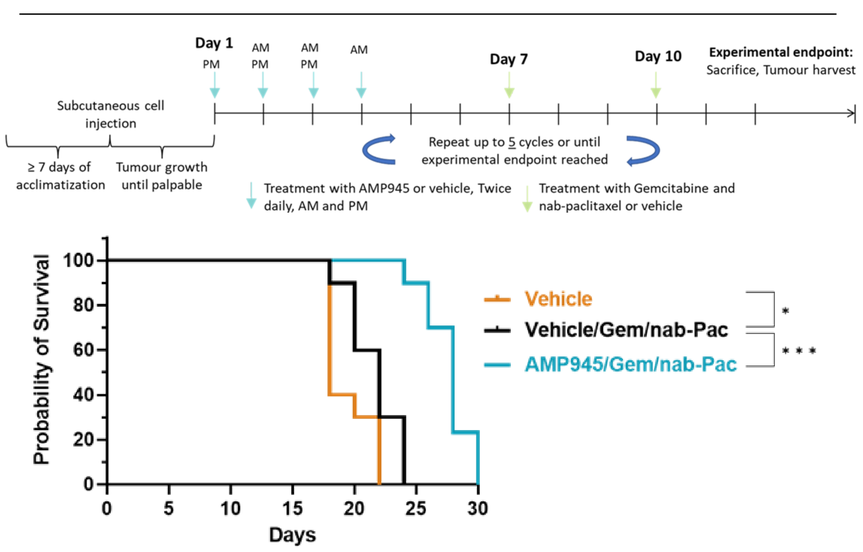


Figure 4: Dosing schedule and Kaplan-Meier survival for KPC Tumour-bearing mice treated with vehicle, pulsed AMP945, gemcitabine and nab-paclitaxel

* p < 0.05 ** p < 0.01 ***p≤ 0.001 ****p≤ 0.0001

AMP945 Clinical Development

Phase 1 Clinical trail for AMP945 in healthy volunteers

A randomized, double-blind, placebo-controlled single ascending dose (SAD) and multiple ascending dose (MAD) Phase 1 clinical trial of AMP945 has been completed in healthy volunteers. In the trial, AMP945 showed excellent safety, tolerability, and pharmacokinetic properties. Importantly, AMP945 demonstrated dose- and exposure-dependent pharmacodynamic evidence of target engagement.

In the Phase 1 study, target engagement was an exploratory analysis measured by the inhibition of Y397-FAK (p-FAK) in skin punch biopsies. Figure 5 shows the change in p-FAK from baseline according to dose for volunteers after daily dosing for 1 week. p-FAK levels were reduced by AMP945 in a roughly dose proportional manner.

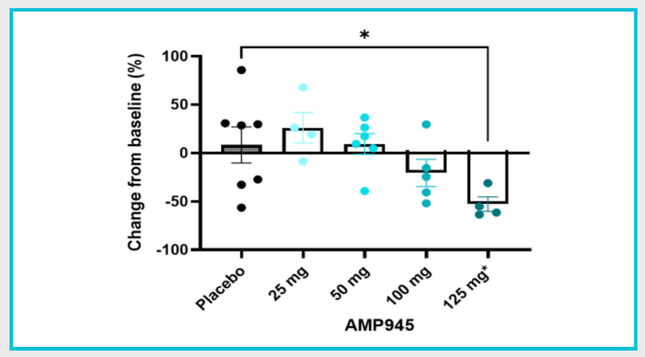
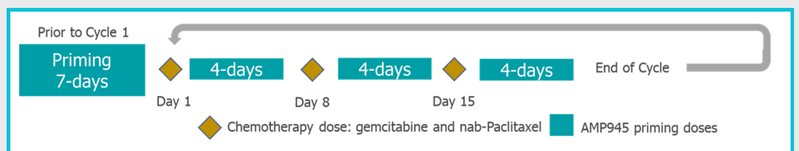


Figure 5: Dose dependent decrease in pFAK levels in skin biopsies

Phase 1b/2 AMP945 in Combination With Nab-paclitaxel and Gemcitabine for Treatment of Pancreatic Cancer

Amplia's recently initiated Phase 1b/2a clinical trial (ACCENT, NCT05355298) is assessing a pulsed dosing regimen of AMP945 in combination with gemcitabine and nab-paclitaxel standard of care as first-line therapy in patients with advanced pancreatic cancer. In the ACCENT trial, patients will receive a one-week oral loading dose of AMP945 and will be pulse-dosed for four days prior to administration of gemcitabine and nab-paclitaxel, given according to a standard treatment schedule. Once daily oral dosing has anticipated benefits in terms of limitation of risk of acquired resistance, minimal potential for drug-drug interactions, adherence to therapy, and allows patients to self-administer AMP945 with the aim of potentiating response to standard of care chemotherapy.



- Potentiates response to standard of care chemotherapy
- Limits risk of acquired resistance
- Reduces potential for drug-drug interactions
- Patients can self-administer AMP945

ACCENT Status

The trial is underway at seven sites in Melbourne, Sydney and Brisbane. The Phase 1b (dose-ranging) portion is progressing well and anticipated to complete in mid-2023. The Phase 2a portion is planned to extend into additional sites in Australia as well as sites in South Korea.

For more information visit: www.ampliatx.com/site/clinical-trial

References:
Pharmacodynamics of AMP945, a potent and selective Focal Adhesion Kinase inhibitor, in normal healthy volunteers. Lambert et. al. 2022 AACR Presentation.
Intravital imaging technology guides FAK-mediated priming in pancreatic cancer precision medicine according to Merlin status. Murphy et al., Sci. Adv. 2021; 7
Focal adhesion kinase priming in pancreatic cancer, altering biomechanics to improve chemotherapy. Murphy et. al., Biochem Soc Trans (2022) 50 (4): 1129–1141.
Increased Survival in Pancreatic Cancer with nab-paclitaxel plus Gemcitabine. Von Hoff et. al., N Engl J Med 2013; 369:1691-1703