ABN 16 165 160 841

ASX RELEASE **9th October 2023**

AACR OVARIAN CANCER CONFERENCE PRESENTATION

HIGHLIGHTS

- *Data from preclinical studies in ovarian cancer presented at premier international conference in Boston, USA.*
- *Results indicate that Amplia's proprietary FAK inhibitor narmafotinib (AMP945) performs better than standard-of-care in models of chemotherapy-resistant high-grade serous ovarian cancer*
- *Data from these studies support clinical study of narmafotinib in ovarian cancer – with plans now commencing with leading international cancer specialists*

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 ovarian cancer models, was presented at the **American Association for Cancer Research (AACR) Special Conference In Cancer Research: Ovarian Cancer** meeting, held in Boston, USA over the weekend. The poster describes research with narmafotinib (AMP945) conducted by the company's collaborators at the University of California, San Diego (UCSD), and was presented by lead researcher Prof Dwayne Stupack.

The data presented clearly demonstrates that narmafotinib is active in mouse models of chemotherapy-resistant ovarian cancer with improved tumour growth inhibition activity and tolerability compared to a PARP inhibitor (niraparib), the current standard-of-care agent for this chemotherapy-resistant patient population. Moreover, narmafotinib showed promising activity in a model where niraparib therapy is ineffective. These results build on previous research by Prof. Stupack and his collaborators showing that activity of the FAK enzyme is upregulated in chemotherapy-resistant ovarian cancer and that FAK inhibition resensitises the cancer to standard-of-care chemotherapy and immunotherapy as well.

Lead researcher Prof Dwayne Stupack stated: "PARP inhibitors are now widely used in the treatment of high-grade serous ovarian cancer (HGSOC) and work well in a subset of patients with what's known as homologous recombinant deficient (HRD) HGSOC – at least until drug resistance occurs. We have shown in our preclinical models that narmafotinib (AMP945) has better activity across the non-HRD disease, and importantly works in PARP inhibitor-resistant disease as well. Moreover, it appears to be very well tolerated, which is important for a drug that will be taken daily."

A copy of the presentation, entitled '*Maintenance therapy inhibition of ptk2 [FAK] yields decreased disease in preclinical models of HRP/HRD models of recurrent HGSOC*' is attached to this announcement.

Amplia CEO and MD, Dr Chris Burns commented: "The research results presented today by Prof. Stupack are extremely exciting and clearly demonstrate that our best-in-class FAK inhibitor narmafotinib has significant potential in the treatment of ovarian cancer. Given that over 1000 women in Australia die each year of this disease, there is a clear need for better treatment, and plans

are now underway to work with local and international ovarian cancer specialists to initiate a clinical trial of narmafotinib in ovarian cancer patients.

“The clinical potential of FAK inhibition in ovarian cancer was demonstrated earlier this year with the first-generation FAK inhibitor defactinib showing promising activity in patients with low-grade serous ovarian cancer. Our preclinical results in models of high-grade disease, which represents over 90% of all ovarian cancer patients, further underscore the potential role of FAK inhibitors in treatment of this disease.”

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

- End -

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.

Maintenance therapy inhibition of ptk2 yields decreased disease in preclinical models of HRP/HRD models of recurrent HGSOC

Breana Hill MD, **Ioana Bondre** MD, **Elise Tahon** MS, **Meryem Soylu** MD, **Duygu Ozmadenci** PhD, **Xiao Lei Chen** MS, **Sarah Kinkel** PhD, **Terrie-Anne Cock** PhD, **Chris Burns** PhD, **David Schlaepfer** PhD, **Michael McHale** MD, **Dwayne Stupack** PhD

University of California San Diego Moores Cancer Center & Amplia Therapeutics

High grade serous ovarian cancer remains the most lethal of the gynecologic malignancies, in part, because of the high incidence of recalcitrant and rapidly recurring disease. Disease recurrence is now better controlled due to maintenance therapy with PARP inhibitors, particularly in homologous repair deficient tumors. Efficacy in homologous repair proficient tumors represents an unmet need. We previously demonstrated that inhibitors of protein tyrosine kinase 2 (ptk2), a gene that is frequently gained in HGSOC, compromises the expression of tumor repair genes, decreases stemness, and limits immune evasion [1] . The low toxicity of ptk2 inhibitors appears to be well suited for a maintenance role. Here, we tested the effect of ptk2 inhibition in two preclinical models of maintenance therapy. In a homologous repair proficient model (KMF), and in a PARP inhibitor resistance model (HGS2), ptk2 inhibitor treatment yielded lower tumor burden, fewer solid tumors, and decreased bloody ascites accumulation relative to treatment with Niraparib.

The low toxicity and overall efficacy provides strong support for future clinical trials with ptk2 inhibitors, in a maintenance role, for patients with HGSOC.

Overview:

HGSOC standard of care (debulking accompanied by taxane and platinum) has a ~80% initial success rate. This creates a challenge for new clinical approaches.

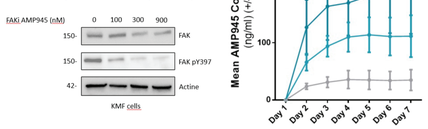
It remains unclear whether standard of care alters tumors, rendering them recalcitrant to further therapy. While PARP inhibitor therapy has shown great success in the maintenance role among BRCA deficient patients, HRP tumors lack an effective tx.

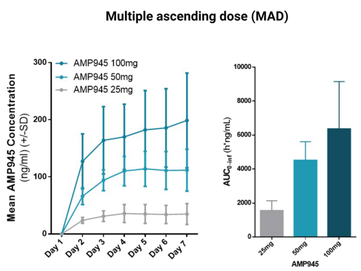
Seventy-two percent of HGSOC patients have gains or amplifications in the PTK2 gene encoding focal adhesion kinase [1]. FAK is a hub kinase that promotes migration, angiogenesis, resistance to platinum, cell stemness and immunosuppression.

Second Generation FAK inhibitors with improved specificity, low toxicity, and pharmacokinetics appropriate for maintenance therapy (QD), are now available [2].

AMP 945 Summary

- *1-6 hours to max*
- *15.7-23.4h half life*
- *Steady state by day 5*

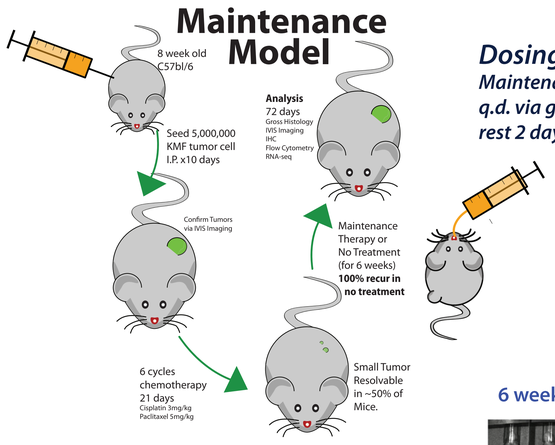




KMF cells are an aggressive in vivo-derivative of ID8 which exhibit further spontaneous genomic alterations, including gains in kras, myc and FAK (ptk2) genes [1].

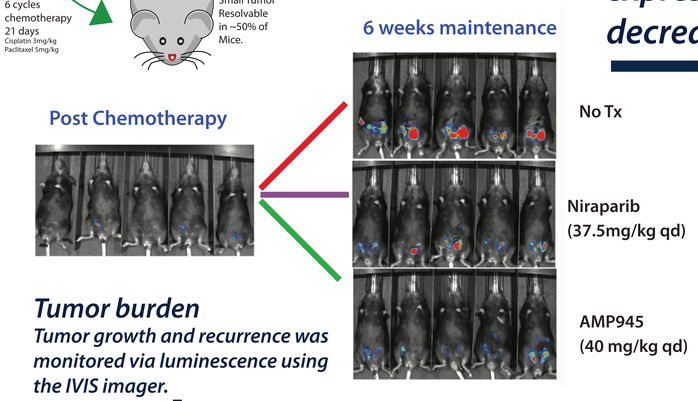
KMF cells have no mutation or loss of BRCA1 or 2.

KMF exhibit platinum resistance and recur in 100% of mice following standard of care chemotherapy.



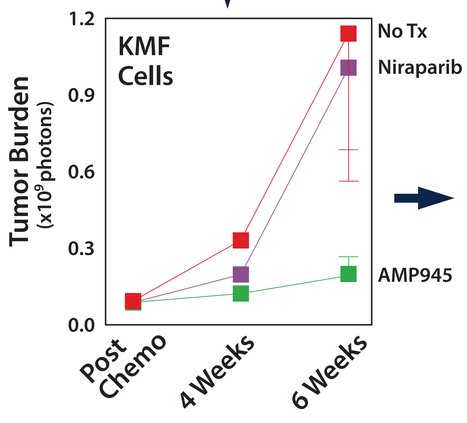
Dosing

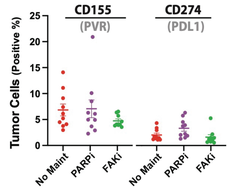
Maintenance therapies administered q.d. via gavage x5 days, rest 2 days.



Tumor burden

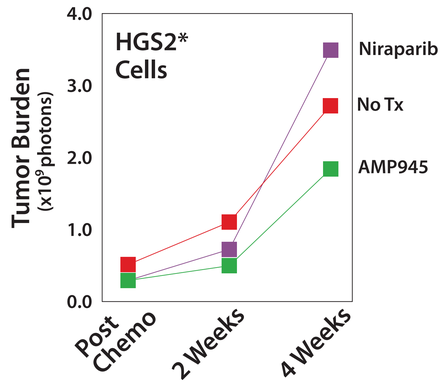
Tumor growth and recurrence was monitored via luminescence using the IVIS imager.





Lavage IP cavity

Evaluate whether FAK Maintenance alters Checkpoint Protein Expression on recovered tumors (as established in chemo-naive mice [4]).



Maintenance Model : HGS2 Cells

(Balkwill Lab)

HGS2 cells are trp53-/-, brca-/- and pten-/- [3]. Our HGS2 cells are resistant to PARP, with an IC50 ~ 100μM, which provides a good model for evolved PARPi Resistance.

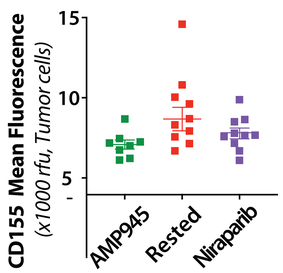
AMP945 maintenance treatment

attenuates HGS2 tumor progression better than Niraparib ($p<0.05$) in this model.

AMP945 maintenance treatment was associated with decreased KMF tumor burden, lack of ascites, trended decreased fraction of tumors expressing tumor checkpoint proteins (CD155, PDL1) with significantly decreased surface abundance.

Adverse Events

AMP945	Rested	Niraparib	
9	10	10	N
0	2	0	Bloody Ascites
0	2	2	Clear Ascites
0	2	2	Solid tumors
0	0	2	Weight Loss (>15%)



References

[1] Diaz Osterman CJ, Ozmadenci D, Kleinschmidt EG, Taylor KN, Barrie AM, Jiang S, Bean LM, Sulzmaier FJ, Jean C, Tancioni I, Anderson K, Uryu S, Cordasco EA, Li J, Chen XL, Fu G, Ojalill M, Rappu P, Heino J, Mark AM, Xu G, Fisch KM, Kolev VN, Weaver DT, Pachter JA, Győrffy B, McHale MT, Connolly DC, Molinolo A, Stupack DG, Schlaepfer DD. FAK activity sustains intrinsic and acquired ovarian cancer resistance to platinum chemotherapy. Elife. 2019 Sep 3;8:

[2] CT511 - A phase 1 trial of AMP945 (ACTRN12620000894998) A potent and selective focal adhesion kinase inhibitor, in healthy volunteers. John Lambert*, Christopher J. Burns, Mark Devlin, Nicole Kruger, Jason Lickliter, Mark Sullivan, Warwick Tong. Amplia Therapeutics, Melbourne, Australia, NMK Consulting, Melbourne, Australia, Nucleus Network, Melbourne, Australia, Medicines Development for Global Health, Melbourne, Australia

[3} Maniati E, Berlato C, Gopinathan G, Heath O, Kotantaki P, Lakhani A, McDermott J, Pegrum C, Delaine-Smith RM, Pearce OMT, Hirani P, Joy JD, Szabova L, Perets R, Sansom OJ, Drapkin R, Bailey P, Balkwill FR. Mouse Ovarian Cancer Models Recapitulate the Human Tumor Microenvironment and Patient Response to Treatment. Cell Rep. 2020 Jan 14;30(2):525-540.e7. doi: 10.1016/j.celrep.2019.12.034. PMID: 31940494; PMCID: PMC6963791.e47327. doi: 10.7554/eLife.47327. PMID: 31478830; PMCID: PMC6721800.

[4] Ozmadenci D, Shankara Narayanan JS, Andrew J, Ojalill M, Barrie AM, Jiang S, Iyer S, Chen XL, Rose M, Estrada V, Molinolo A, Bertotto T, Mikulski Z, McHale MC, White RR, Connolly DC, Pachter JA, Kuchroo VK, Stupack DG, Schlaepfer DD. Tumor FAK orchestrates immunosuppression in ovarian cancer via the CD155/TIGIT axis. Proc Natl Acad Sci U S A. 2022 Apr 26;119(17):e2117065119. doi: 10.1073/pnas.2117065119. Epub 2022 Apr 25. PMID: 35467979; PMCID: PMC9169934.

Delaney JR, Patel CB, Willis KM, Haghighiabyaneh M, Axelrod J, Tancioni I, Lu D, Bapat J, Young S, Cadassou O, Bartakova A, Sheth P, Haft C, Hui S, Saenz C, Schlaepfer DD, Harismendy O, Stupack DG. Haploinsufficiency networks identify targetable patterns of allelic deficiency in low mutation ovarian cancer. Nat Commun. 2017 Feb 15;8:14423. doi: 10.1038/ncomms14423. PMID: 28198375; PMCID: PMC5316854.