

ASX RELEASE

15 September 2021

Amplia Provides Updated Investor Presentation

Amplia Therapeutics Limited (ASX: ATX) (“Amplia” or the “Company”) today released a new investor slide deck which provides further information on the Company’s technology and its plans to initiate Phase 2 clinical studies of AMP945 in pancreatic cancer and pulmonary fibrosis.

The attached presentation provides the following:

- A summary of Amplia’s technology, targeted therapeutic indications and competitive landscape
- Summary results from the Company’s recently completed Phase 1 clinical trial of AMP945
- Information on the Phase 2 clinical trial the Company is planning in pancreatic cancer patients
- Preclinical data underpinning the Company’s planned Phase 2 clinical studies in pancreatic cancer and pulmonary fibrosis

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

- End -

For Further Information

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CEO and Managing Director

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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 pancreatic and ovarian cancer. FAK also plays a significant role in a number of chronic diseases, such as idiopathic pulmonary fibrosis (IPF).

Amplia Therapeutics

September 2021

Amplia Therapeutics Limited



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There can be no assurance or guarantee that actual outcomes will not differ materially from these statements. The data and results pertaining to clinical subjects used in this presentation are illustrative of medical conditions and outcomes associated with potential applications of Amplia’s acquired product pipeline. Actual results from clinical trials may vary from those shown.

Amplia Therapeutics is developing new drugs for the treatment of cancer and fibrosis



Investment highlights



- Two Focal Adhesion Kinase (FAK) inhibitors with activity profiles supporting multiple therapeutic opportunities
 - Clear differentiation from other FAK inhibitors in development
- AMP945 has completed a Phase 1 trial in 56 volunteers and was shown to have an excellent safety and tolerability profile
- Phase 2 clinical trials planned in cancer and fibrosis
- Highly experienced management team, Board and advisor network
- Solid track record in delivery against timelines and budgets
- Collaboration in place with world leading FAK-biology group at the Garvan Institute



Management Team



John Lambert

PhD, GAICD
MD & CEO

- Medicines Development for Global Health
- Biota Pharmaceuticals
- Univ of Melbourne, ANU, Harvard University



Mark Devlin

PhD, MBA
CSO

- Cancer Therapeutics CRC
- Director Translational Cancer Biology
- Assoc Prof Pharmacology
- Univ of Melbourne, UNSW

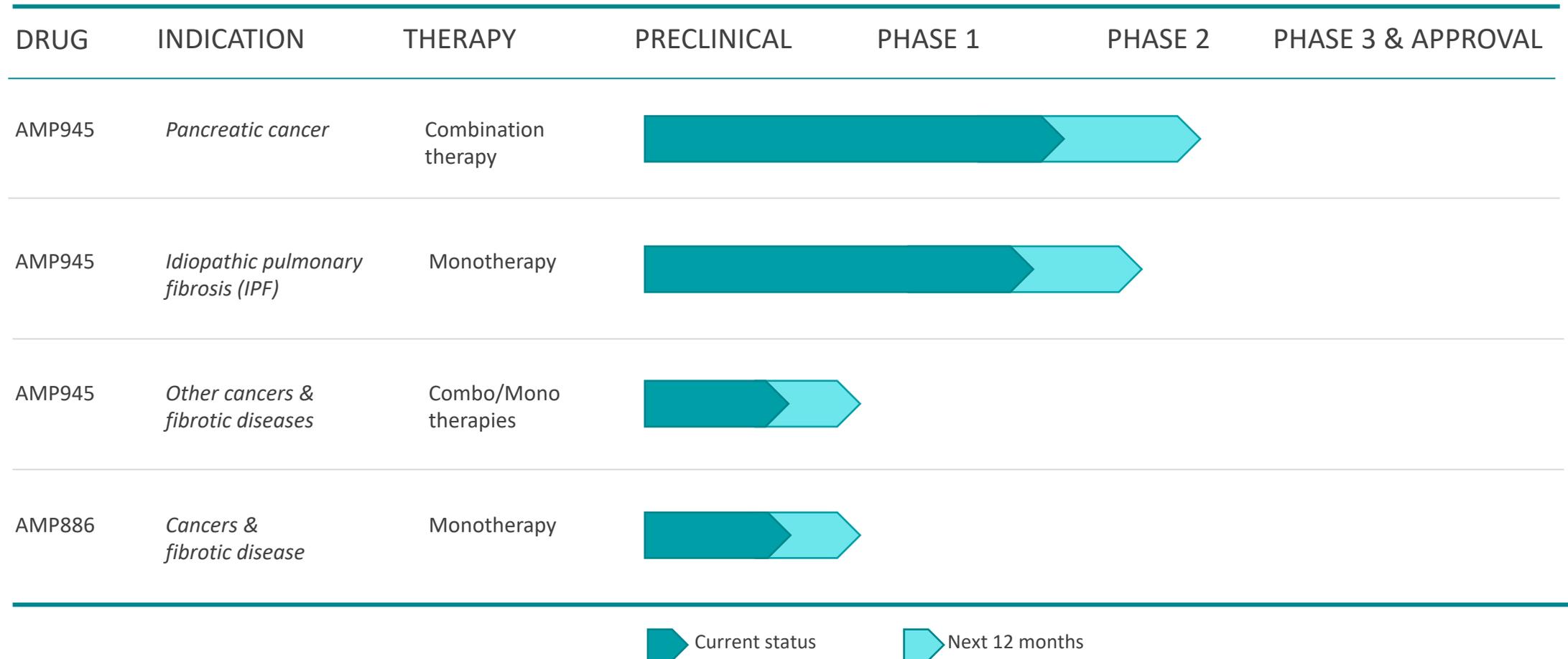


Rhiannon Jones

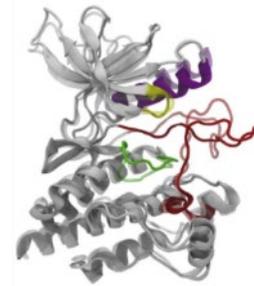
PhD, BSc (Hons)
Director, Operations

- Cancer Therapeutics CRC
- 10Y in medical research and R&D management
- Univ of Adelaide, Governance Institute of Australia

Amplia's pipeline



Why is FAK a good target for drug development?



Focal Adhesion Kinase (FAK)

Indication

FIBROTIC DISEASES

SOLID CANCERS

Opportunities

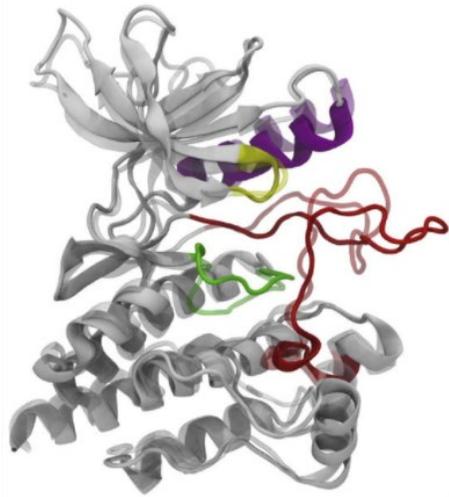
Monotherapy

- Lung fibrosis
- Liver fibrosis (NASH)
- Renal fibrosis
- Wound healing

Combination Therapy

- Pancreatic cancer
- Ovarian cancer
- Breast cancer
- Hepatocellular carcinoma
- Melanoma
- Gastric cancer
- Lung cancer

Targeting cancer's defence mechanisms



Focal Adhesion Kinase (FAK)

Fibrosis
FAK helps establish and maintain the dense, fibrotic tissue around cancers
Immune activity
FAK triggers the release of signaling molecules (cytokines) which suppress the immune system
Cell migration
FAK regulates cell migration that is involved in the formation of secondary cancers (metastases)



FAK is involved in many cancer defence mechanisms that reduce the effectiveness of cancer drugs

Increased FAK activity is found in many, difficult-to-treat, solid cancers

Elevated levels of FAK in cancers are associated with poor outcomes



Amplia is investigating the use of FAK inhibitors (FAKi's) to disrupt cancer defence mechanisms, making them more responsive to cancer drugs

**Remove the shield.
Deliver the blow.**

Amplia's target indications



Pancreatic Cancer

- 60,000 new diagnoses and 48,000 deaths from pancreatic cancer in the US each year
- Difficult-to-treat cancer that is often surrounded by a protective, fibrotic stromal layer
- Less than 20% patients eligible for surgery – chemo main treatment
- Few new therapies approved and most patients treated with cytotoxic chemotherapy drugs

AMP945 was awarded Orphan Drug Designation by the US FDA for use in treating Pancreatic Cancer in March 2020

Idiopathic Pulmonary Fibrosis (IPF)

- Affects 130,000 in the US and ~3M people worldwide
- Devastating, progressive disease caused by the build up of fibrotic tissue in the lungs
- Only two drugs approved which slow progression but are unable to stop the disease
- With treatment, median survival time is 3-5 years

AMP945 was awarded Orphan Drug Designation by the US FDA for use in treating Idiopathic Lung Fibrosis in May 2020

Why Target Pancreatic Cancer and Pulmonary Fibrosis?



Pancreatic Cancer	Pulmonary Fibrosis
Preclinical data provides rationale for clinical study in this disease	
Data from Garvan collaboration shows AMP945 enhances the efficacy of standard of care (SOC) in animal models	Positive impact of AMP945 in the bleomycin mouse model accepted by clinical advisors as appropriate rationale
Gateway indication to other fibrotic cancers/fibrotic diseases	
Ovarian cancer; Breast cancer; Hepatocellular carcinoma; Melanoma; Gastric cancer; Lung cancer	Liver fibrosis (NASH); Renal fibrosis; Wound healing
Unmet need, market size and partnering landscape	
Unmet need where incremental improvements to standard of care will be widely accepted	Unmet need with limited treatment options available
2021 Total Addressable Market (TAM) \$2B, forecast to grow to \$5.4B by 2029*	2021 TAM \$2.2B, forecast to grow to \$4.6B by 2027**
Treatments are expected to evolve with kinase inhibitors becoming a more significant drug class in this indication	Vibrant partnering landscape for fibrosis drugs

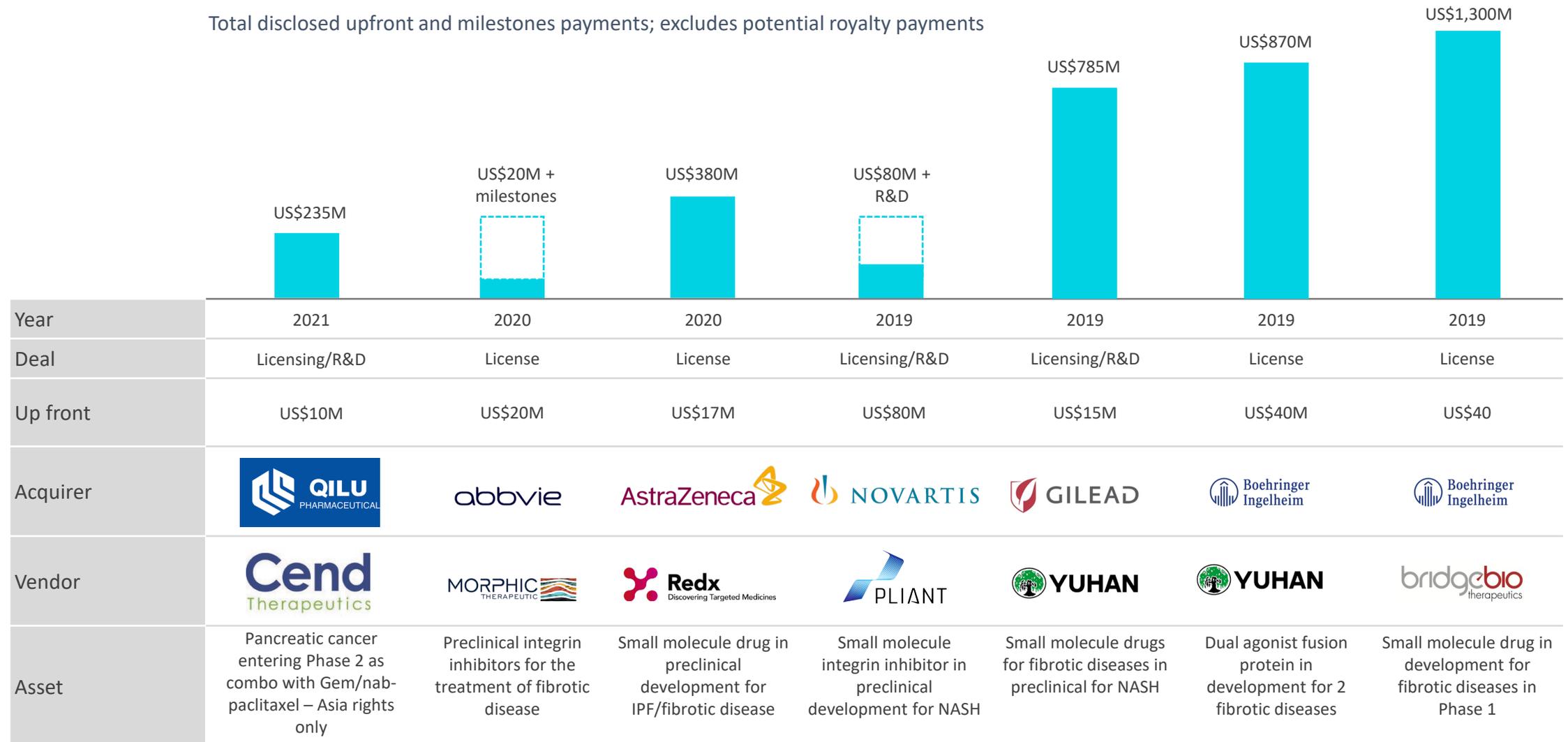
* GlobalData, *Pancreatic Cancer –Opportunity Analysis and Forecasts to 2029* (2020)

** ResearchAndMarkets, *Idiopathic Pulmonary Fibrosis - Global Market Trajectory & Analytics*, 2021

Recent deals for anti-fibrotic and pancreatic cancer drugs



Total disclosed upfront and milestones payments; excludes potential royalty payments



Product differentiation



Company	FAKi	FAK Selectivity	Pancreatic Cancer		Fibrosis
			First Line	Combo with	
Amplia	AMP945	✓✓✓	✓	Gem/nab-paclitaxel	✓
Verastem	defactinib	✓	✗	Pembrolizumab	✗
InxMed	IN10018	✓✓	✗	Pembrolizumab KN046	✗

Amplia’s AMP945 is differentiated from its competitors by

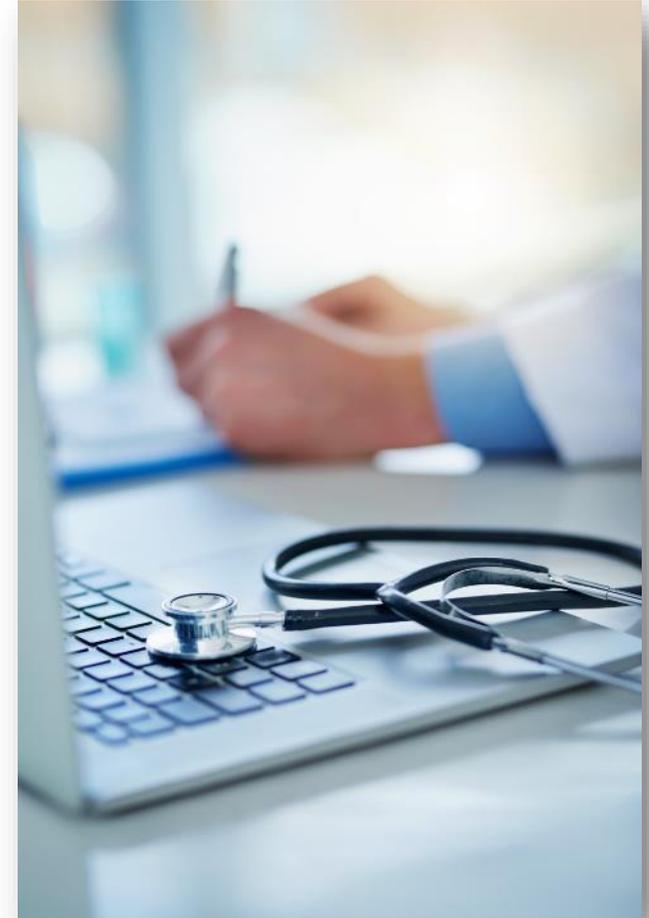
1. Exquisite FAK selectivity
2. Pairing with first-line therapy
3. Combination with gemcitabine/nab-paclitaxel, an approved pancreatic cancer therapy
4. AMP945’s clinical safety profile is consistent with development in fibrosis indications

Clinical Development of AMP945

Phase 1 trial of AMP945 completed in May 2021



- Trial execution:
 - Commenced in October 2020 - completed May 2021
 - Recruited in 56 healthy volunteers aged 18 - 65
 - Single site in Melbourne Australia, Nucleus Network
- Phase 1 trial components:
 - Single Ascending Doses
 - Multiple Ascending Doses
 - Food Effect
 - Pharmacokinetics
 - Pharmacodynamics



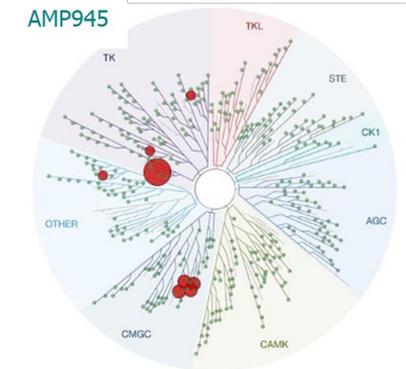
Results



- AMP945 was safe and well-tolerated at all doses tested
 - No Serious Adverse Events. AEs generally mild and considered not related to AMP945
- No evidence of food effect on oral absorption
- Pharmacokinetics support once-a-day oral dosing
- Supports advancing AMP945 into Phase 2 clinical trials
 - Planning for Phase 2 trial in pancreatic cancer and pulmonary fibrosis underway
 - On track to initiate first Phase 2 clinical trial in Q1 2022



Selectivity of AMP945 is underlined by a favourable clinical safety profile



Summary of Treatment Emergent Adverse Events from Amplia's Phase 1 trial of AMP945

	Single Dose					Multiple Dose			
	Cohort 1 AMP945 X mg (N=6)	Cohort 2 AMP945 2X mg (N=6)	Cohort 3 AMP945 4X mg (N=6)	Cohort 4 AMP945 8.3X mg (N=6)	Pooled Placebo (N = 8)	Cohort 1 AMP945 Y mg (N = 6)	Cohort 2 AMP945 2Y mg (N=6)	Cohort 3 AMP945 4Y mg (N = 6)	Pooled Placebo (N = 6)
Severity Rating	Number of Events					Number of Events			
Mild	1	1	5	1	3	7	6	4	5
Moderate	0	2	1	0	0	2	0	0	0
Severe	0	0	0	0	0	0	0	0	0

N = Number of volunteers per Cohort

Significance of data from Phase 1 clinical trial



- AMP945's safety profile is significant because it supports:
 - Clinical trials in combination with chemotherapy in first-line pancreatic cancer patients
 - Clinical trials as a single-agent in idiopathic pulmonary fibrosis (IPF) patients
- AMP945's excellent pharmaceutical profile is significant because:
 - Once-a-day oral administration delivers therapeutically relevant levels of AMP945 in the bloodstream
 - Patients can self-administer capsules of AMP945, supporting both oncology and longer-term once-daily dosing for chronic fibrotic disease



Phase 2 Clinical Trial in Pancreatic Cancer Patients

Amplia's collaboration with the Garvan Institute



- Collaboration is focussed on enhancing efficacy of current standards of care
 - Differentiated from competitors who are seeking to install activity into drugs with no known efficacy in this disease
- Garvan Provides
 - Exclusive access to current know-how and first rights to new IP
 - Access to clinician network and clinical sample analysis
- Amplia provides
 - Translational opportunity for Garvan's basic research
 - Research funding
- To date, we have shown that
 - AMP945 improves efficacy of standard of care chemotherapy in an animal model of pancreatic cancer
 - Underlying biology consistent with enhanced survival effect



Key questions

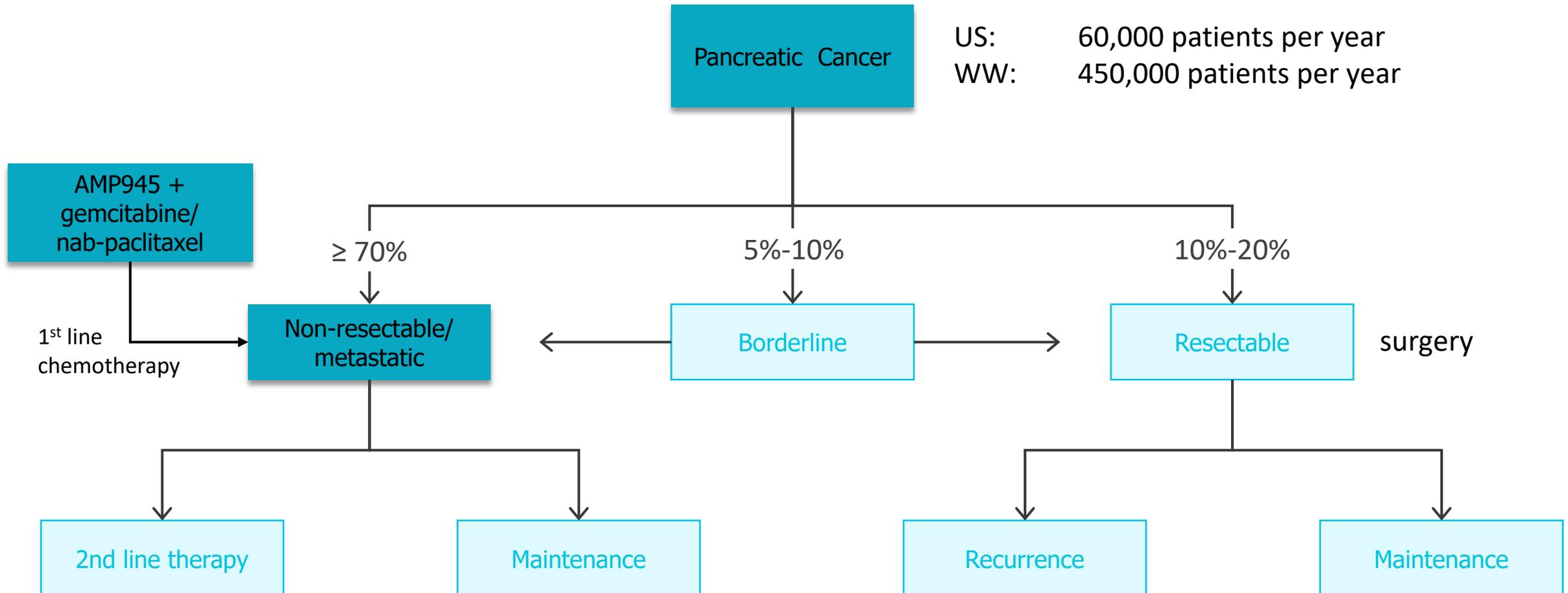


Does AMP945 enhance the efficacy of gemcitabine and nab-paclitaxel in patients with advanced pancreatic cancer?

If AMP945 does enhance the efficacy of gemcitabine and nab-paclitaxel, how does this manifest clinically?

Which patients respond best to AMP945 combined with gemcitabine and nab-paclitaxel?

AMP945 will be integrated into first-line therapy



Gilbert, J. W., Wolpin, B., et al., 'Borderline Resectable Pancreatic Cancer: Conceptual Evolution and Current Approach to Image-Based Classification', *Ann Oncol*, 28 (2017), 2067-76.

Benefits of developing AMP945 as 1st line therapy



Largest patient population: >70% newly diagnosed patients

- Largest addressable market opportunity
- Large patient pool to recruit from for clinical trial

Patients better able to respond

- treatment naïve
- less likely to have developed resistance
- better overall health

Minimal impact on current clinical practice

- integrates with established experience
- opportunity to enhance available treatment
- will help acceptance and adoption

“With the exception of two targeted agents, which exhibited minimal or no overall survival benefit (erlotinib and olaparib), standard treatments are limited to conventional chemotherapies.”

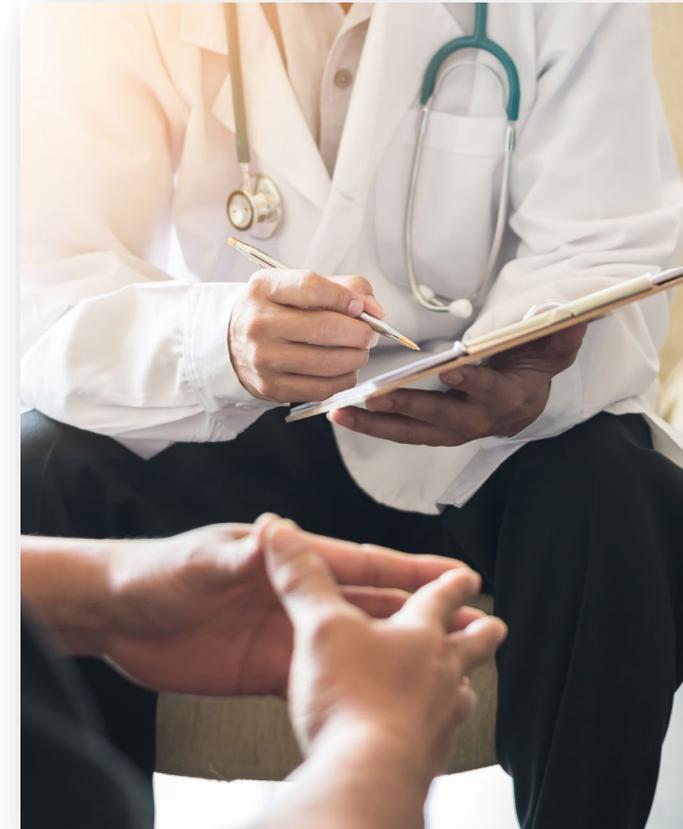
“There have been no paradigm-shifting advances beyond combination chemotherapy in the pancreatic cancer field over the past two decades. This contrasts with many other common cancers, which have benefited from impactful targeted therapies.”

A comprehensive analysis of clinical trials in pancreatic cancer; what is coming down the pike? *Oncotarget* 2020, 11:3489-3501

Efficacy Endpoints for Phase 2 Trial



- Primary Efficacy Endpoint – ORR
 - Widely used
 - Able to support accelerated approvals*
 - Sensitive endpoint – mitigates risk of false positive result
- Secondary Endpoints – DoR, PFS, OS, CR, Symptoms, Pharmacokinetics
 - Alternate measures of efficacy
 - Initial assessment of effect sizes
- Exploratory Endpoints – pFAK, CA19-9, fibrosis markers
 - Signals of response
 - Predictive biomarkers



* FDA, 'Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics - Guidance for Industry', (2018).

ORR: Objective Response Rate; DoR: Duration of Response; PFS: Progression Free Survival; OS: Overall Survival; CR: Complete Response; CA19-9: Carbohydrate antigen 19-9

Schedule



Activity	CY2021		CY2022				CY2023				CY2024			
	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Pancreatic Cancer														
Drug Product Development	▶													
Drug Interaction Studies	▶													
HREC Filing		◆												
IND filing				◆										
Patient Recruitment			▶											
Interim Analysis								◆						
Pulmonary Fibrosis														
Extended Toxicology			▶											
Patient Recruitment							▶							

HREC: Human Research Ethics Committee
 IND: Investigational New Drug

Preclinical Data

AMP945 is the most selective FAK inhibitor currently in clinical development

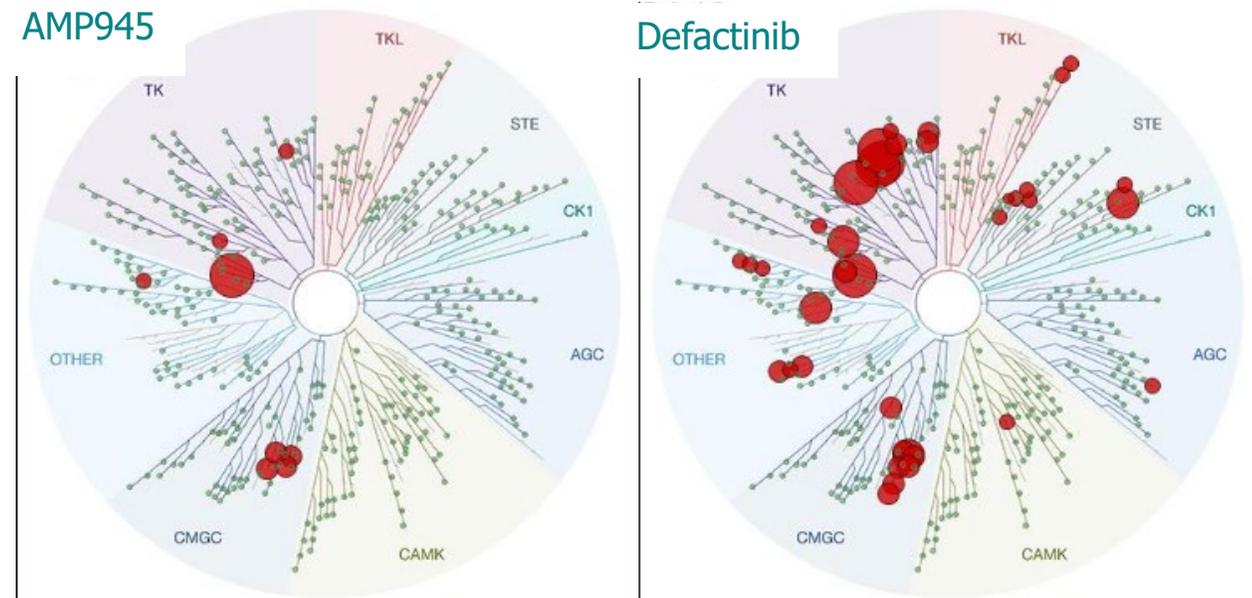


Non-specific kinase inhibition often leads to clinical side effects

AMP945 is currently the most selective FAK inhibitor in clinical development

Number of kinases targeted in addition to FAK with *in vitro* IC₅₀ < 1μM:

- **AMP945**: 3 (468 kinase tested)
- IN10018: 4 (262 kinase tested)
- Defactinib: 9 (468 kinase tested)

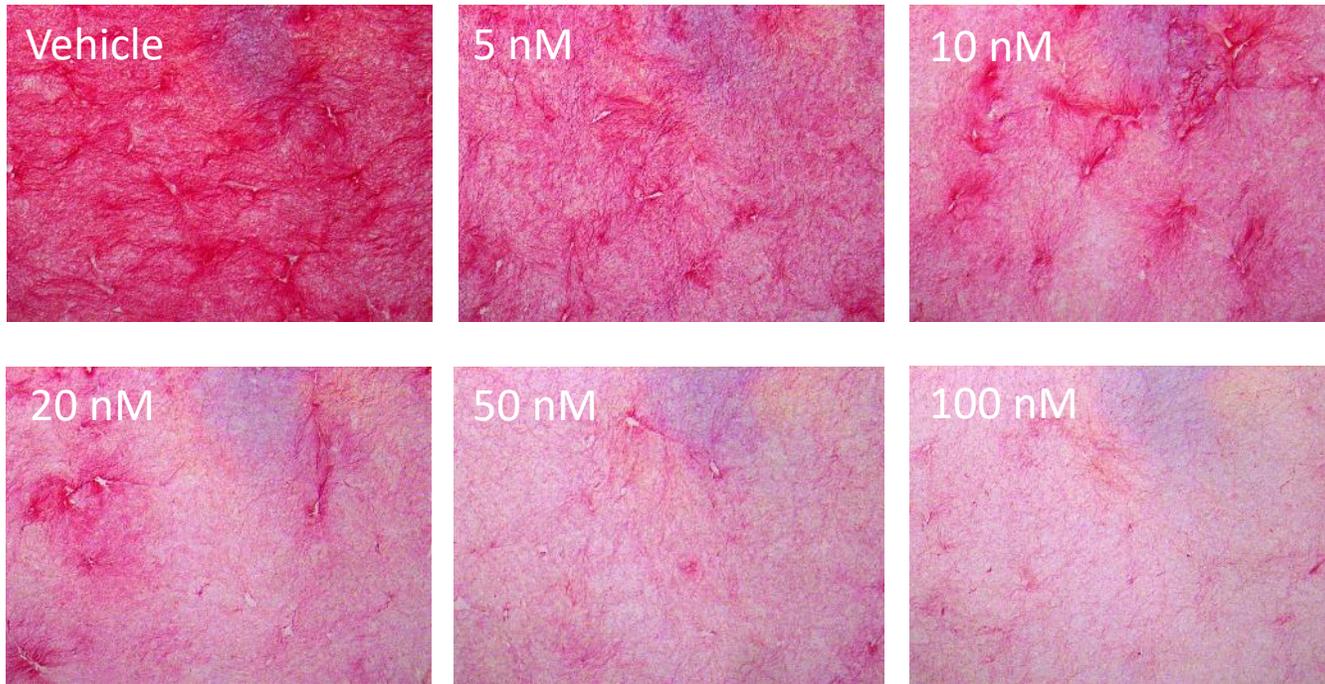


Attributes	AMP945
Kinases inhibited (IC ₅₀ nM)	FAK (0.9)
CYP inhibition	> 20 μM all isoforms
Glutathione trapping	negative
Comments	Highly selective for FAK across 468 kinase screen

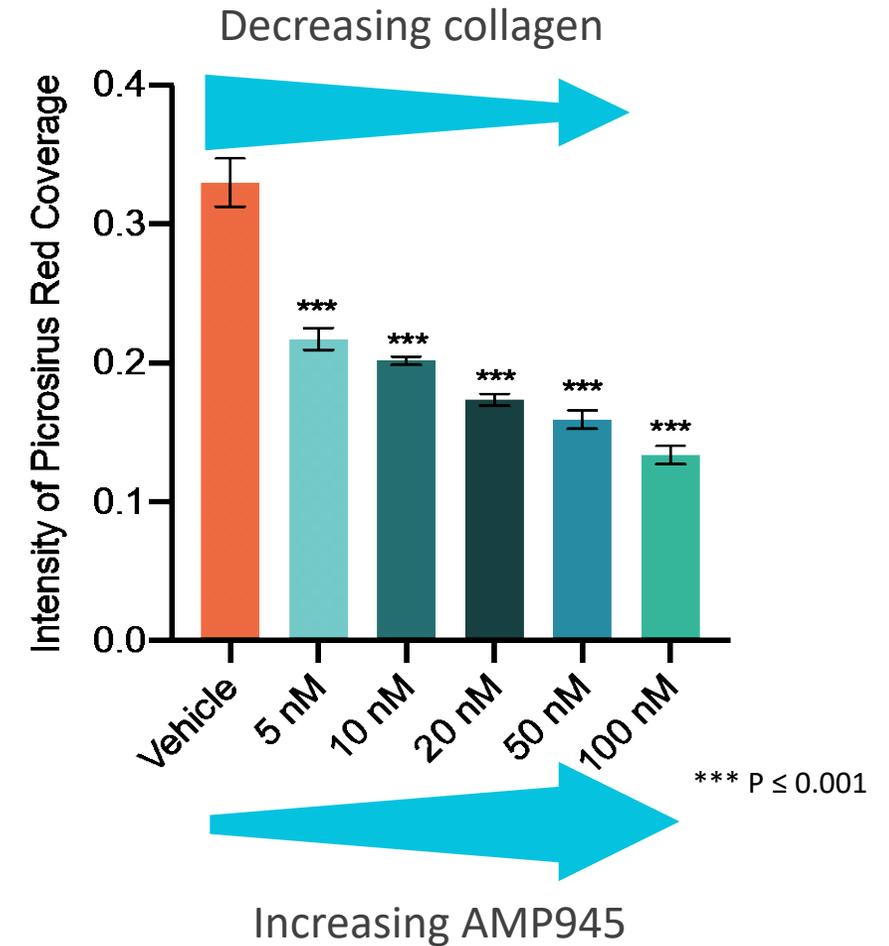
AMP945 inhibits deposition of collagen



Picosirius red staining for total collagen

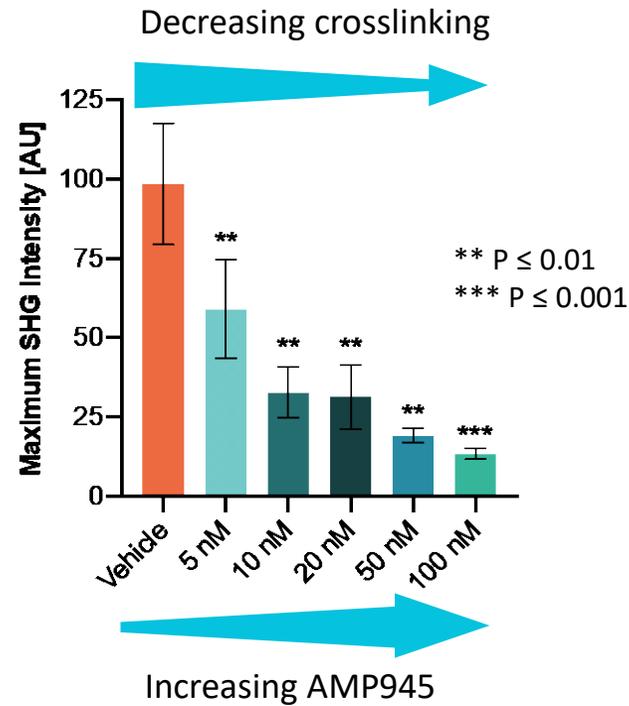
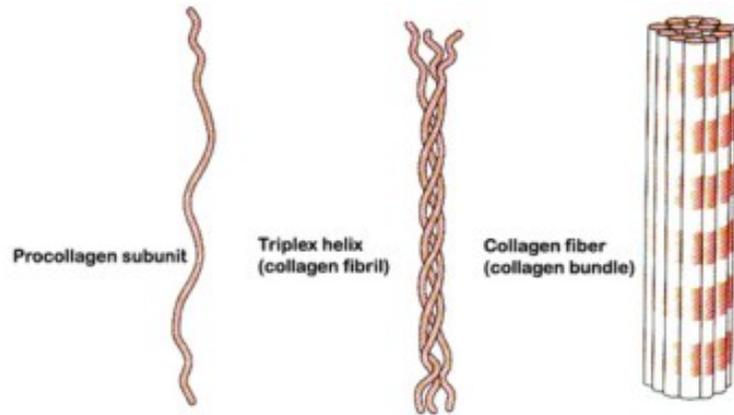


- Fibroblasts lay down new collagen
- Collagen is a key component of fibrotic tissue
- AMP945 inhibits fibroblasts, causing less new collagen to be deposited

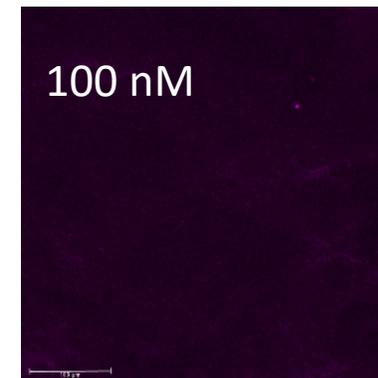
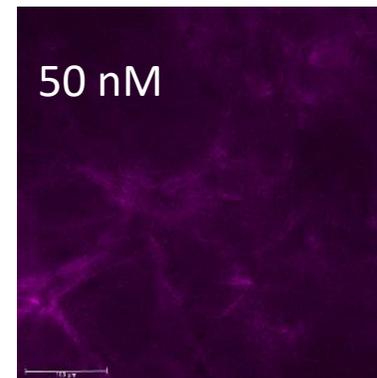
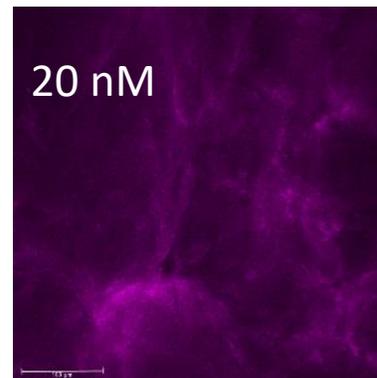
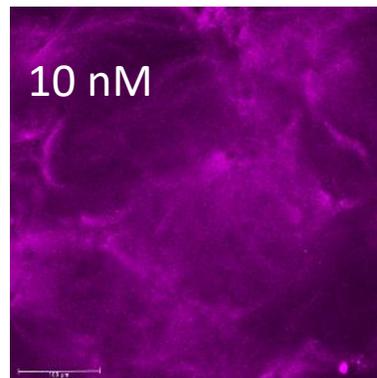
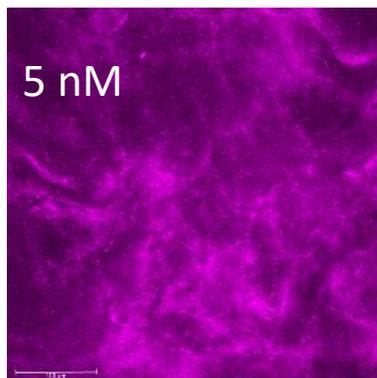


Studies conducted in the laboratory of Professor Paul Timpson (Garvan)

AMP945 blocks collagen cross-linking



- Crosslinking of collagen is required for the formation fibrotic tissues
- AMP945 inhibits collagen cross-linking in a dose-dependent manner

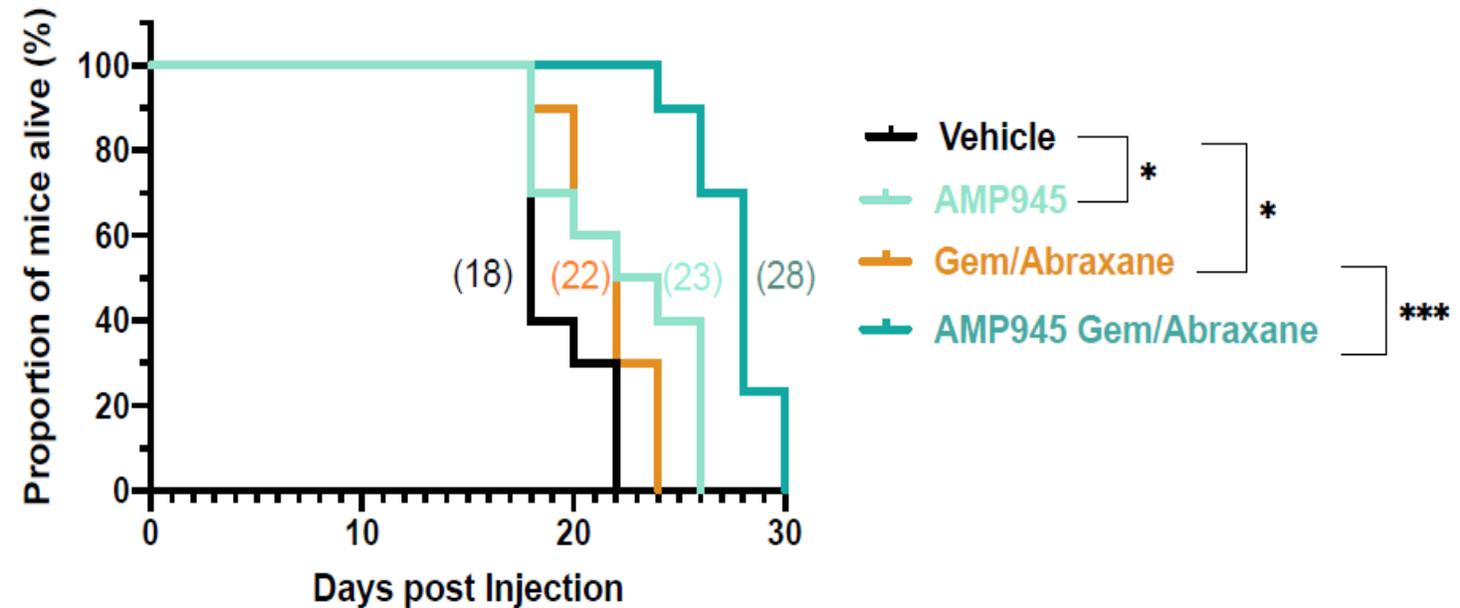


AMP945 improves survival in pancreatic cancer model



Survival in the KPC mouse model of pancreatic cancer

- 25% improvement in survival when added to standard of care ($p \leq 0.001$)
- KPC is a highly aggressive animal model of human pancreatic cancer
- Demonstrates pharmaceutical activity of AMP945 translates into survival benefit



"A 25% improvement in survival in this model is very impressive and a level of improvement that we rarely see"

AMP945 treats and prevents lung fibrosis



Bleomycin animal model of lung fibrosis

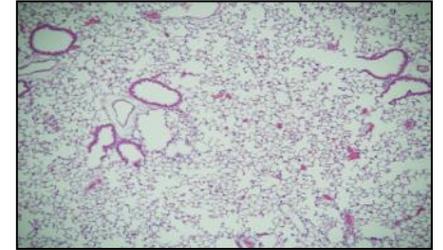
PREVENTION

- AMP945 administered before onset of fibrosis
- Evaluating ability of AMP945 to prevent fibrosis from becoming established

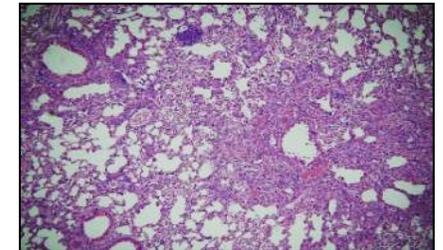
TREATMENT

- AMP945 administered after onset of fibrosis
- Evaluating ability of AMP945 to treat established fibrosis

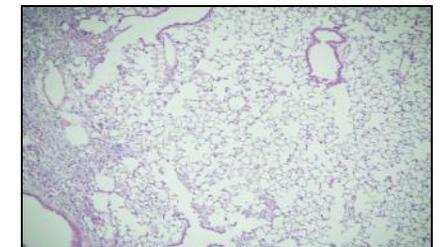
control – healthy lung



bleomycin – fibrotic lung



bleomycin + AMP945

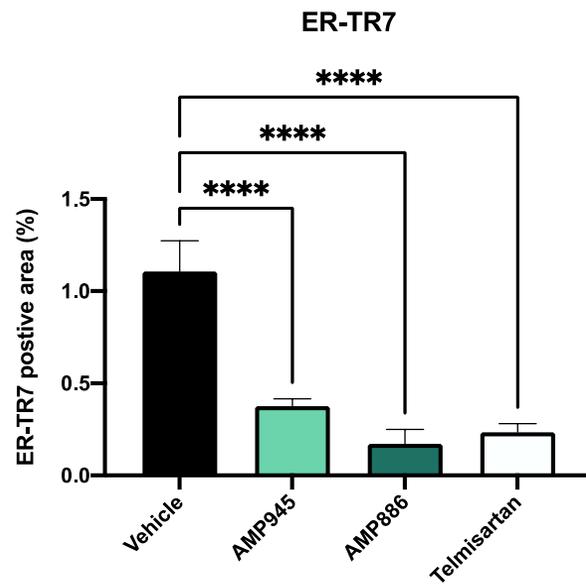


- FAK has a pivotal role in the biochemical pathways regulating both the development and progression of fibrosis in the lungs
- AMP945 both prevents and reverses the fibrosis in the industry-standard disease model for lung fibrosis

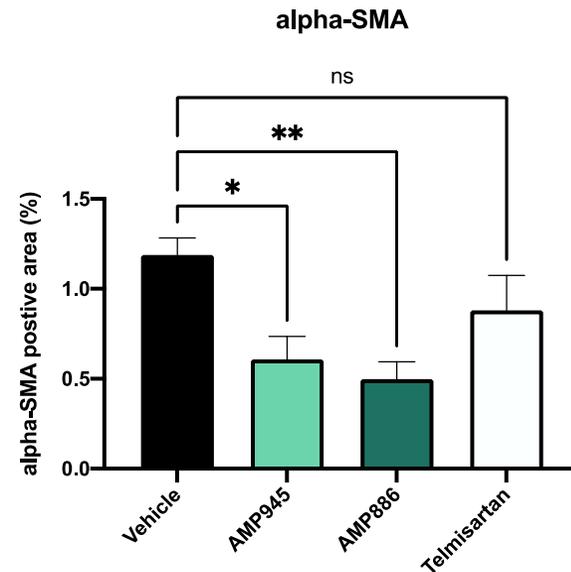
AMP945 and AMP886 are effective in an animal model of NASH*



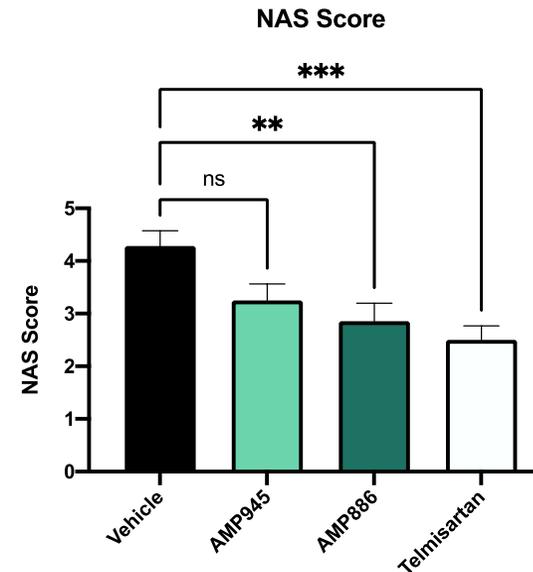
Fibroblast marker



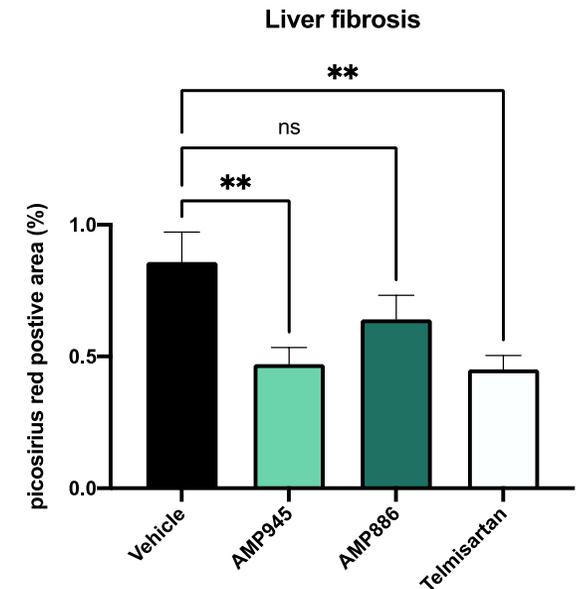
Fibroblast activation



NASH symptoms



Fibrosis



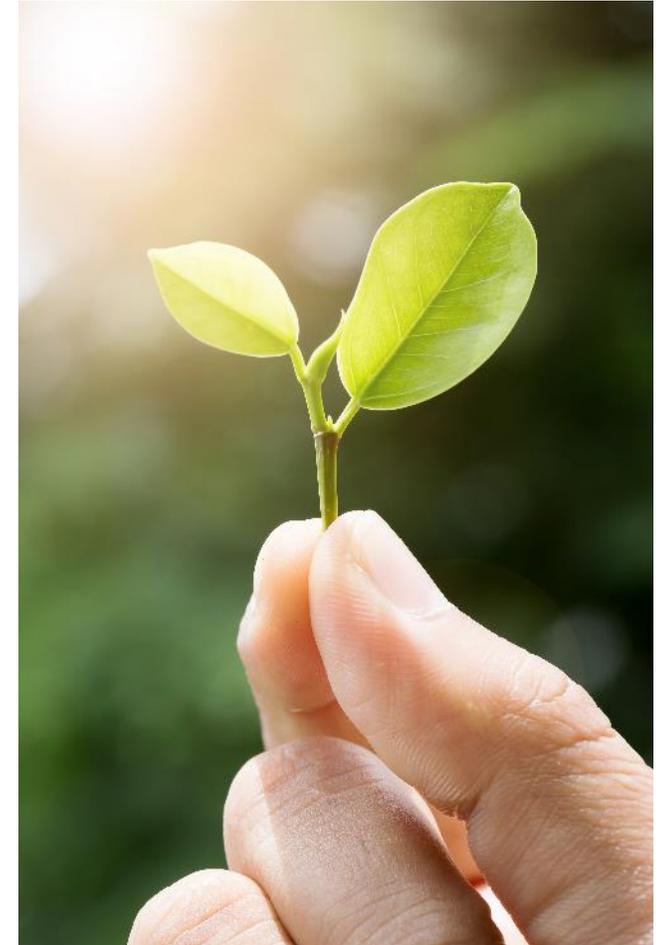
* P ≤ 0.05
** P ≤ 0.01
*** P ≤ 0.001
**** P ≤ 0.0001

* Non-alcoholic steatohepatitis

Summary



- Successful Phase 1 trial completed
 - AMP945 now poised for development in 2 therapeutic areas
- Phase 2 trial in **pancreatic cancer** expected to commence recruitment in Q1 2022
- Phase 2 trial in **pulmonary fibrosis** expected to commence recruitment in Q3 2022
- Preclinical studies ongoing to further expand therapeutic options





ampliatx.com