RECRUITING

Trial Name and ID	Site Details	Target Population	Key Eligibility and Treatment Details
ACCENT (AMP945-PC-201) NCT05355298 *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* Amplia Therapeutics	**Epworth PI** A/Prof Sumitra Ananda **Epworth locations** • Richmond *(Richmond)* • Freemasons *(East Melbourne)* • Eastern *(Box Hill)*	Metastatic (Stage IV) pancreatic ductal adenocarcinoma **Line of therapy** First-line	**Treatment** • Focal adhesion kinase (FAK) inhibitor AMP945 (oral) given prior to dosing with nab-paclitaxel and gemcitabine in first-line setting **Key Eligibility** • ECOG 0-1 • Has received no previous radiotherapy, surgery, chemotherapy, or investigational therapy for the treatment of metastatic disease • Radiotherapy within 14 days prior to run-in *Click here for full eligibility criteria*
SPEAR ACTRN12621001347853 *A phase 2, open-label, single-arm sulfasalazine monotherapy trial of progression-free survival in patients with pancreatic adenocarcinoma* Omico.	**Epworth PI** Dr Allan Zimet **Epworth locations** • Richmond *(Richmond)* • Freemasons *(East Melbourne)*	Locally advanced (Stage III) unresectable or Metastatic (Stage IV) pancreatic ductal adenocarcinoma **Line of therapy** Second-line +	**Treatment** • Sulfasalazine monotherapy (oral) in ≥ second-line setting **Key Eligibility** • ECOG 0-1 • Has had one-line of systemic therapy for advanced disease. Patients who have had two lines of systemic therapy or are intolerant of second-line treatment may be eligible after consultation with the study Investigators • Radiotherapy within 28 days prior to Day 1 *Click here for full eligibility criteria*
DIRECT-InspIRE Australia ACTRN12621000955819 *Investigation of the safety and efficacy of irreversible electroporation (IRE) using the NanoKnife® System in patients with unresectable stage 3 pancreatic cancer who have received 3 months of chemotherapy* WEHI brighter together	**Epworth PI** Mr Brett Knowles **Epworth locations** • Freemasons *(East Melbourne)*	Locally advanced (Stage III) unresectable **Line of therapy** First-line	**Treatment** • Irreversible Electroporation (IRE) with the NanoKnife system (surgical) **Key Eligibility** • ECOG 0-1 • Newly diagnosed and has only received a single line of therapy for at least 3 months prior to enrolment (no more than 6 months). Must have received either modified FOLFIRINOX or gemcitabine-based chemotherapy • Has not undergone prior radiation therapy or surgical resection for treatment of pancreatic cancer *Click here for full eligibility criteria*

IN FOLLOW-UP / CLOSED (NOT RECRUITING)

Trial Name and ID	Site Details	Target population	Key Eligibility and Treatment details
YH003004 NCT04481009 *A phase II, multi-center, open-label study to evaluate the safety and efficacy of YH003 in combination with Toripalimab (anti-PD-1 mAb) in patients with unresectable/ metastatic melanoma and pancreatic ductal adenocarcinoma (PDAC).* EUCURE BIOPHARMA	**Epworth PI** A/Prof Sumitra Ananda **Epworth locations** • Richmond *(Richmond)* • Freemasons *(East Melbourne)*	Locally advanced (Stage III) unresectable or Metastatic (Stage IV) pancreatic ductal adenocarcinoma **Line of therapy** Second-line +	**Treatment** • YH003 (recombinant humanized agonistic CD40 IgG2 mAb) in combination with Toripalimab (anti-PD-1 mAb) with or without nab-paclitaxel + gemcitabine **Key Eligibility** • ECOG 0-1 • Had confirmed progressive disease during treatment with first line standard of care of chemotherapy per local standard. • Must not have received any anticancer therapy or another investigational agent within 4 weeks or 5 half-lives before the first dose of the study IP. *Click here for full eligibility criteria*
ASCEND ACTRN12621001290886 *A Randomised, double-blinded phase II study of gemcitabine and nab-paclitaxel with CEND-1 or placebo in patients with untreated metastatic pancreatic ductal adenocarcinoma* AGITG AUSTRALASIAN GASTRO-INTESTINAL TRIALS GROUP	**Epworth PI** Dr Ross Jennens **Epworth locations** • Richmond *(Richmond)* • Freemasons *(East Melbourne)*	Metastatic (Stage IV) pancreatic ductal adenocarcinoma **Line of therapy** First-line	**Treatment** • Gemcitabine and nab-paclitaxel with CEND-1/LSTA1 or placebo **Key Eligibility** • ECOG 0-1 • Archival tumour tissue for tertiary correlative. Fine needle aspirate (FNA) or brushings will not be accepted. • Prior radiotherapy or major surgery (as defined by local investigator) within 14 days of starting treatment. *Click here for full eligibility criteria*

ASCEND (ACTRN12621001290886)

Key Inclusion Criteria

1. Adults, 18 years or older with histologically confirmed metastatic pancreatic ductal adenocarcinoma or poorly differentiated carcinoma.
2. Measurable disease according to RECIST 1.1.
3. Archival tumour tissue for tertiary correlative studies (biopsy or resection of primary or metastasis). Fine needle aspirate (FNA) or brushings will not be accepted.
4. ECOG performance of 0-1
5. Adequate renal and haematological function
6. Adequate hepatic function, defined as:
   Bilirubin <1.5 X ULN (Upper Limit of Normal), AST or ALT greater than or equal to 5x ULN.
   If a person was recently stented with improving bilirubin, the person can be randomised with bilirubin up to 3 x ULN provided chemotherapy is not administered until within the stated thresholds.
7. Willing and able to comply with all study requirements, including treatment, timing and/or nature of required assessments.
8. Study treatment both planned and able to start within 7 days after randomisation
9. Signed, written informed consent.

Key Exclusion Criteria

1. Uncontrolled metastatic disease to the central nervous system. To be eligible, known CNS metastases should have been treated with surgery and/or radiotherapy and the patient should have been receiving a stable dose of steroids for at least 2 weeks prior to randomisation, with no deterioration in neurological symptoms during this time.
2. Prior chemotherapy or investigational anti-cancer therapy for metastatic pancreatic adenocarcinoma. Prior treatments with curative intent or for locally advanced disease are allowed, provided the last dose of chemotherapy was administered more than 6 months prior to randomisation.
3. Prior radiotherapy or major surgery (as defined by local investigator) within 14 days of starting treatment.
4. Any unresolved toxicity greater than or equal to NCI CTCAE Grade 2 from previous anti-cancer therapy with the exception of alopecia, vitiligo and the laboratory values defined in the inclusion criteria. Participants with greater than or equal to Grade peripheral neuropathy are not allowed.
5. Concurrent use of any other anti-cancer therapy including chemotherapy, targeted therapy, immunotherapy or biological agents.
6. Known allergy or hypersensitivity to any of the study drugs and excipients.
7. Any significant active infection, including chronic active hepatitis B, hepatitis C, or HIV. Participants with known Hepatitis B/C infection will be allowed to participate providing evidence of viral suppression has been documented and the patient remains on appropriate anti-viral therapy.
8. History of prior or synchronous malignancy within 2 years prior to randomisation, except:
a. Malignancy that was treated with curative intent and for which there has been no known active disease for greater than or equal to 2 years prior to randomisation.
b. Curatively treated non-melanoma skin cancer, cervical cancer in situ, superficial transitional cell carcinoma of the bladder, stage 1 endometrial carcinoma, prostatic intraepithelial neoplasia, low-grade papillary thyroid cancer, untreated localised very low risk or low risk prostate cancer under observation.
9. Concurrent illness, including severe infection that may jeopardise the ability of the person to undergo the procedures outlined in this protocol with reasonable safety.
10. Neuroendocrine pancreatic carcinoma.
11. Life expectancy of less than 3 months.
12. Pregnancy, lactation, or inadequate contraception. Women must be post-menopausal, infertile, or use a reliable means of contraception. Women of childbearing potential must have a negative pregnancy test done within 7 days prior to randomisation. Men must use a reliable means of contraception.
13. Serious medical or psychiatric conditions that might limit the ability of the person to comply with the protocol.

ACCENT (NCT05355298)

Key Inclusion Criteria

1. Provide written informed consent prior to any study procedures and agree to adhere to all protocol requirements.
2. Aged at least 18 years at the time of consent.
3. Confirmed histological or cytological diagnosis of advanced pancreatic adenocarcinoma that is:
   Part A: metastatic or not surgically resectable.
   Part B: metastatic, with initial diagnosis of metastatic disease ≤6 weeks prior to Baseline.
4. Has measurable disease, defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded) as >20 mm with conventional techniques or as >10 mm with spiral CT scan.
5. Eligible for treatment with nab-paclitaxel and gemcitabine as standard of care therapy.
6. Eastern Cooperative Oncology Group (ECOG) Performance Score of 0-1, sustained on two separate assessments: the first at least 2 weeks prior to the 1st dose of AMP945 and the 2nd within 72 hours prior to the 1st dose of AMP945. Participants not maintaining an ECOG Performance Score of 0-1 at the second assessment will be excluded from participation.
7. Has a life expectancy of >3 months.
8. Adequate organ function, as defined by the laboratory results below (samples must be obtained ≤14 days prior to study drug administration):
   a) Haematology:
      (i) Absolute neutrophil count (ANC) ≥1.5 × 109/L;
      (ii) Platelet count ≥100,000/mm3 (100 × 109/L);
      (iii) Haemoglobin (Hgb) ≥9 g/dL.
   b) Serum chemistry:
      (i) Aspartate transaminase (AST) (SGOT), ALT (SGPT) ≤2.5 × upper limit of normal range (ULN), unless liver metastases are clearly present, then ≤5 × ULN is allowed;
      (ii) Total bilirubin ≤ULN;
      (iii) Creatinine <1.5 x upper limit of normal (ULN) or estimated glomerular filtration rate (eGFR) >60 mL/min/1.73m2 (calculated using the Cockcroft-Gault equation).
   c) No clinically significant abnormalities in coagulation results.
   d) No clinically significant abnormalities in urinalysis results.
9. Agree to use contraception according to protocol

Key Exclusion Criteria

1. Pregnant or breast-feeding, or plans to become pregnant during the study.
2. Has received any investigational medicinal product (IMP) within 30 days or 5 half-lives (whichever is longer) prior to Day -8.
3. Known brain metastases, unless previously treated and well-controlled for at least 3 months (defined as clinically stable, no oedema, no steroids and stable in 2 scans at least 4 weeks apart).
4. Gastrointestinal condition that could interfere with the swallowing or absorption of study medication.
5. Part A: Has received prior systemic treatments for pancreatic cancer, except those given in the adjuvant setting, and with recurrence more than 6 months after completion of curative/adjuvant treatment.
6. Part B: Has received no previous radiotherapy, surgery, chemotherapy, or investigational therapy for the treatment of metastatic disease. Prior treatment with 5-FU or gemcitabine administered as a radiation sensitizer in the adjuvant setting is allowed, provided at least 6 months have elapsed since completion of the last dose and no lingering toxicities are present. Participants having received cytotoxic doses of gemcitabine or any other chemotherapy in the adjuvant setting are not eligible for this study.
7. History of malignancy other than in situ cancer or basal or squamous cell skin cancer in the last 5 years.
8. Major surgery, other than diagnostic surgery (i.e., surgery done to obtain a biopsy for diagnosis without removal of an organ), within 4 weeks prior to Day -8.
9. Known human immunodeficiency virus (HIV) and/or history of Hepatitis B or C infections or known to be positive for Hepatitis B surface antigen (HBsAg) or Hepatitis C Antibody.
10. Known history of myocardial infarction, coronary stenting, stroke, or cerebrovascular accident within 6 months prior to the first dose of study drug.
11. Focal palliative radiotherapy (e.g., to a bony metastasis) within the 14 days prior to Run-in, or more extensive radiotherapy within 28 days prior to Run-in.
12. History of chronic leukemias (e.g., chronic lymphocytic leukemia).
13. History of interstitial lung disease, history of slowly progressive dyspnoea and unproductive cough, sarcoidosis, silicosis, idiopathic pulmonary fibrosis, pulmonary hypersensitivity pneumonitis or multiple allergies.

14. History of connective tissue disorders (e.g., lupus, scleroderma, arteritis nodosa).
15. Clinical signs of active infection and/or a temperature of > 38.0°C at the time of Screening or Baseline. Study entry may be deferred at the discretion of the Principal Investigator (PI).
16. Currently using warfarin.
17. Administration of a live virus vaccine in the 4 weeks prior to Day -8 or plans to receive a live virus vaccine during the study.
18. Clinically significant allergies to AMP945, nab-paclitaxel or gemcitabine (or any of their excipients), including hypersensitivity reactions to human albumin, that are not likely to be well controlled with premedication or other supportive measures.
19. Exhibiting any of the conditions or events outlined in the Contraindications or Special Warnings and Precautions sections of the nab-paclitaxel and/or gemcitabine package inserts.
20. Peripheral neuropathy > Grade 1.
21. Corrected QT interval using Fridericia's correction (QTcF) > 460 ms for males and >480 ms for females.
22. Any clinically relevant medical, social, or psychiatric conditions, or any finding during Screening, which in the Investigator's opinion may put the participant at unacceptable risk or interfere with the study objectives.
23. Prior treatment with AMP945.

SPEAR (ACTRN12621001347853)

Key Inclusion Criteria

1. Aged >=18 years old.
2. Histologically or cytologically confirmed locally advanced (Stage III) unresectable or metastatic (Stage IV) PDAC.
3. Adequate archival tissue for comprehensive genomic profiling.
4. Disease must have progressed after one-line of standard fluoropyrimidine- or gemcitabine-based chemotherapy for advanced disease. Treatment break within the upfront chemotherapy regimen is considered the same line of therapy and is permitted.
5. Have had one-line of systemic therapy for advanced disease. Patients who have had two lines of systemic therapy or are intolerant of second-line treatment may be eligible after consultation with the study Chief Investigators.
6. ECOG performance status score of 0-1.
7. Life expectancy >12 weeks.
8. Measurable disease as defined by RECIST version 1.1.
9. Presence of tumour amenable to a second biopsy.
10. Adequate haematological indices as defined by:
    a. Absolute neutrophil count >=1.0 x 10^9/L
    b. Haemoglobin >=100 g/L
    c. Platelet count >=100 x 10^9/L
    d. Bilirubin <1.5x ULN
    e. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <1.5x ULN; or <5.0x ULN if liver metastases are present
    f. International normalised ratio (INR) <1.3 in the absence of anticoagulation therapy.
11. Adequate renal function, as defined by Creatinine Clearance (CrCl) >=50mL/min using Cockcroft formula.
12. Women of childbearing potential and men must use effective contraception during the study and for at least 90 days after the last dose of study medication. Women of childbearing potential must have a negative screening serum pregnancy test.
13. Ability to adhere to the study visit schedule and understand and comply with all protocol requirements and instructions from study staff.
14. Provision of written informed consent.

Key Exclusion Criteria

1. Diagnosis of other histology types other than ductal adenocarcinoma, including but not limited to pancreatic acinar cell carcinoma, well-differentiated neuroendocrine tumour, neuroendocrine carcinoma, or lymphoma. Mixed histology with predominantly adenocarcinoma component is eligible.
2. Uncontrolled diabetes, defined as HbA1c >10% in previous 3 weeks.
3. Pregnant or breastfeeding.
4. Major surgery within 28 days prior to Day 1. Biliary stent placement or endoscopic procedure is permitted.
5. Radiation therapy within 28 days prior to Day 1.
6. Uncontrolled central nervous system or brain metastases.
7. Uncontrolled hypertension (systolic blood pressure [SBP] >180mmHg or diastolic blood pressure [DBP] >105mmHg).
8. New York Heart Association Class III or IV congestive heart failure.
9. Current clinical or laboratory evidence of active or uncontrolled infection.
10. History of uncontrolled severe asthma or atopic dermatitis requiring hospitalization.
11. Concomitant advanced solid or haematological malignancy with an expected prognosis that is worse than the index pancreatic adenocarcinoma.
12. Active major gastrointestinal bleeding.
13. Known hypersensitivity or allergic reactions to salicylates or sulphonamide derivatives, including antibacterial sulphonamides, oral hypoglycaemics and thiazides.
14. Known intestinal or urinary obstruction or porphyria.
15. Participation in studies of investigational products within 28 days prior to Day 1, or 5 half-lives, whichever is longer.
16. Clinically significant and uncontrolled medical condition considered a high risk for participation in an investigational study or a likelihood that the potential participant will be unable to comply with protocol requirements and complete the trial (e.g. emphysema requiring supplemental oxygen, poorly controlled arrhythmia, psychiatric illness, Alzheimer's disease).
17. Current abuse of alcohol or drugs.

DIRECT-InspIRE (ACTRN12621000955819)

Key Inclusion Criteria

1. Patient has a diagnosis of unresectable Stage 3 pancreatic ductal adenocarcinoma cancer cytologically or pathologically confirmed as per American Joint Committee on Cancer (AJCC) staging criteria.
2. Patient is newly diagnosed and has only received a single line of therapy for at least 3 months prior to enrolment. They must have received either modified FOLFIRINOX or gemcitabine-based chemotherapy.
3. Patient has a tumour evaluated as Stage 3 according to National Comprehensive Cancer Network (NCCN) guidelines, based on radiographic imaging or exploratory surgery.
4. Maximum axial tumour dimension of less than or equal to 3.5cm, after receiving at least three months of treatment with a modified FOLFIRINOX or gemcitabine-based regimen.
5. Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
6. Patient has an American Society of Anaesthesiologists (ASA) classification of physical health status of 1 or 2.

Key Exclusion Criteria

1. Patients who at 3 months after induction chemotherapy have evidence of disease progression.
2. Patients who have undergone prior radiation therapy or surgical resection for treatment of pancreatic cancer.
3. Patients who have received IRE for margin accentuation.
4. Patients who are unable to tolerate general anaesthetic with full skeletal muscle blockade.
5. History of another primary cancer within the last 3 years, with the exception of non-melanomatous skin cancer and carcinoma in-situ.
6. Patients who are actively bleeding, anticoagulated, coagulopathy, or have any of the following haematology results:
    a. Haemoglobin <100 g/L without the support of growth factors or transfusion
    b. Absolute neutrophil count <1.5 x 109/L
    c. Platelet count <100 x 109/L
7. Patients with the presence of implanted cardiac pacemakers, defibrillators, electronic devices or implanted devices with metal parts in the thoracic cavity at the time of IRE.
8. Patients with history of epilepsy or other neurological disease.
9. Patients with inadequate organ function:
    a. Patients with Stage 3 (GFR 30 to 44ml/min), 4 (15 to 29ml/min), or 5 (<15ml/min) chronic kidney disease.
    b. Aspartate aminotransferase/alanine aminotransferase >2.5 x upper limit of normal.
    c. Clinically significant cardiovascular disease i.e. active or <12 months since e.g. cerebrovascular accident, myocardial infraction, unstable angina, New York Heart Association grade II or greater congestive heart failure, serious cardiac arrhythmias requiring medications, uncontrolled hypertension.
10. Patients who are pregnant or breastfeeding. Women of childbearing potential (WOCBP) must undergo pregnancy testing.

YH003004 (NCT04481009)

Key Inclusion Criteria

1. Subjects must have the ability to understand and willingness to sign a written informed consent document.
2. Part I dose escalation:
3. Have histologically advanced or cytologically confirmed solid tumor. Have progressed on after treatment with at least one standard therapy or intolerant of the standard therapy.
4. Part II dose expansion:
   Cohort 2A: Histologically or cytologically confirmed unresectable or metastatic melanoma that had confirmed progressive disease during treatment with an anti-PD-1/PD-L1 therapy with or without additional CTLA-4 therapy. Subjects with BRAF activating mutation could have also received a BRAF inhibitor and/or MEK inhibitor regimen prior to anti-PD-1/PD-L1 therapy.
   Cohort 2B, 2C: Subject has histologically or cytologically documented diagnosis of pancreatic ductal adenocarcinoma with unresectable locally advanced/metastatic disease Cohort 2B: had confirmed progressive disease during treatment with first line standard of care of chemotherapy per local standard.
   Cohort 2C: treatment-naïve for unresectable locally advanced/metastatic disease.
5. Subject must have measurable disease by RECIST 1.1. At least 1 unidimensional measurable target lesion per RECIST v1.1 for study Part II expansion cohorts.
6. Subjects must be age 18 years or older.
7. Subjects must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Life expectancy ≥3 months.
8. Subjects must have adequate organ function.
9. Women of reproductive potential must have negative serum beta human chorionic gonadotropin (β -HCG) pregnancy test.

Key Exclusion Criteria

1. Part II Cohort 2A: History of life-threatening toxicity or treatment discontinuation due to related to prior anti-PD-1/PD-L1 and with or without CTLA-4 combination treatment for subjects with unresectable/metastatic melanoma.
2. Subjects must not have another active invasive malignancy.
3. Previous exposure to TNFR such as anti-CD137, OX40, CD27 and CD357 antibodies.
4. Subjects must not have received any anticancer therapy or another investigational agent within the shorter of 4 weeks or 5 half-lives before the first dose of the study treatment.
5. Subjects with a history of ≥ Grade 3 immune-related adverse events resulted from previous immunotherapy.
6. History of clinically significant sensitivity or allergy to monoclonal antibodies and their excipients or known allergies to antibodies produced from Chinese hamster ovary cells, which in the opinion of the Investigator suggests an increased potential for an adverse hypersensitivity to YH003 or Toripalimab. Also history of severe hypersensitivity reaction to Nap-paclitaxel and/or gemcitabine.
7. Primary central nervous system (CNS) malignancies or symptomatic CNS metastases.
8. History of (non-infectious) pneumonitis that required corticosteroids or current pneumonitis, or history of interstitial lung disease.
9. Subjects must not have a known or suspected history of an autoimmune disorder, including but not limited to inflammatory bowel disease, celiac disease, Wegner syndrome, Hashimoto syndrome, systemic lupus erythematosus, scleroderma, sarcoidosis, or autoimmune hepatitis, within 3 years of the first dose of study treatment.
10. Clinically uncontrolled intercurrent illness, including an ongoing or active infection, active coagulopathy, uncontrolled diabetes, psychiatric illness that would limit compliance with the study requirements and other serious medical illnesses requiring systemic therapies.
11. Severe cardiovascular disease including symptomatic congestive heart failure (New York Heart Association class III or IV), unstable angina, uncontrolled hypertension, cardiac arrhythmia, a history of myocardial infarction within 6 months or a history of arterial thromboembolic event and pulmonary embolism within 3 months of the first dose of investigational agent.
12. QTc > 450 ms at baseline; no concomitant medications that would prolong the QT interval; no family history of long QT syndrome.
13. Subjects must not have active infection of human immunodeficiency virus (HIV), hepatitis B, or hepatitis C.
14. Subjects must not have a history of primary immunodeficiency.
15. Subjects from endemic area will be specifically screened for tuberculosis. Subjects with active tuberculosis are excluded.
16. Subjects must not receive concurrent or prior use of an immunosuppressive agent within 4 weeks of the first dose of YH003.
17. Major surgery within 4 weeks prior to study entry and Minor surgery within 2 weeks prior to the first dose of YH003.
18. Subjects must not have received a live attenuated vaccine within 28 days before the first dose of YH003, and subjects, if enrolled, should not receive live vaccines during the study or for 180 days after the last dose of YH003.