CLINICAL TRIAL PORTFOLIO

PANCREATIC CANCER

LaBahn Pancreatic Cancer Program
Hope Innovation Discovery Cure

RESECTABLE AND BORDERLINE RESECTABLE

A. Treatment Naïve
  I. CA19-9 Producer (CA 19-9 > 35 U/mL, when total bilirubin 2 mg/dL)
    a. PANC Trial – Phase II trial of adaptive neoadjuvant therapy
  II. CA19-9 Non-producer & Producer
    a. PANCREAS Trial – Phase II Trial of Tumor Subtype-directed Neoadjuvant Chemotherapy
B. Prior Neoadjuvant Chemotherapy
  I. PROCLAIM – Phase II, mobile application for clinical trial discussions
C. Post Surgical Resection
  I. PROTECT-PANC – Phase II, adjuvant therapy for patients at risk of cancer recurrence

LOCALLY ADVANCED

A. Type A – Potentially Operable
  I. PANCREAS Trial – Phase II Trial of Tumor Subtype-directed Neoadjuvant Chemotherapy
  Type B – Unresectable
  I. NRG-GI011 – Testing Higher Dose Radiation Therapy for Locally Advanced Pancreatic Cancer
B. Post Surgical Resection
  I. PROTECT-PANC – Phase II, adjuvant therapy for patients at risk of cancer recurrence

METASTATIC

A. Phase I and II
  I. NEOGENE-NT-112-301 – Phase I, a master protocol to investigate TCR-Engineered T cells recognizing KRAS mutations in adult subjects with Unresectable, Advanced, and/or Metastatic Solid Tumors.
  II. ASTELLAS-2138-CL-0101 – Phase I/Ib, ASP2138 in Adults with Stomach Cancer or Pancreatic Cancer (check for slot availability)
  IV. IIT-GEORGE-I-PREDICT – Phase I/II, Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy for Patients
  V. COLUMBIA-S9513-CHEMO4METPANC - Phase II, Chemo4METPANC Combination Chemokine Inhibitor, Immunotherapy, and Chemotherapy in Pancreatic Adenocarcinoma
  VI. PROCLAIM – Phase II, mobile application for clinical trial discussions
B. Phase II and III
  I. MOUNTAINTAP-30 – A Randomized, Phase II/III Study Comparing BMS-986504 in Combination With Nab-paclitaxel and Gemcitabine Versus Placebo in Participants With Untreated Metastatic Pancreatic Ductal Adenocarcinoma Harboring Homozygous MTAP Deletion

PANCREATIC NEUROENDOCRINE

I. SWOG-S2012 – Randomized Phase II Trial of First Line Platinum/Etoposide with or without Atezolizumab in Patients with Advanced or Metastatic Poorly Differentiated Extrapulmonary Neuroendocrine Carcinomas (NEC)

RESECTABLE & BORDERLINE RESECTABLE

Clinical Trial Name: Adaptive Modification of Neoadjuvant Therapy Based on Clinical Response in Patients with Localized Pancreatic Cancer (PANC Trial)

Study Design: This is a single arm, Phase II clinical trial utilizing neoadjuvant therapy and surgery for patients with resectable and borderline resectable pancreatic adenocarcinoma which utilizes a total neoadjuvant therapy approach with adaptive modification of the chemotherapy regimen based on radiographic response (CT scan), biochemical response (CA19-9 decline), and performance status (as measured by a short physical performance battery).

NCT#: NCT03322995

Study PI:
Dr. Kathleen Christians

Clinical Research Coordinator:
Lauren Schmitz
Phone: 414-805-5175

Key Inclusion:

- ECOG performance status of < 2
- Histologically confirmed adenocarcinoma of the pancreas
- Clinical stage resectable or borderline resectable pancreatic adenocarcinoma
- Must be CA19-9 producer (pretreatment CA19-9 > 35 U/mL when total bilirubin ≤ 2 mg/dL)

Key Exclusion:

- Received chemotherapy and/or radiation within 3 years prior to study enrollment
- History of prior malignancy except for adequately treated in situ cancer of the cervix or basal cell or squamous cell skin cancer or localized prostate cancer with a normal PSA within the last 3 years

Clinical Trial Name: PurIST Classification-Guided Adaptive Neoadjuvant Chemotherapy by RNA Expression Profiling of EUS SAmples Study (PANCREAS)

Study Design: This is an open-label, single arm, phase II study in patients with resectable and borderline resectable pancreatic cancer. The study intervention involves molecular profiling Purity Independent Subtyping of Tumors (PurIST) subtyping of pretreatment Endoscopic Ultrasound Fine Needle Aspiration (EUS/FNA) samples to determine pancreatic cancer subtype. Neoadjuvant therapy is directed based on the molecular subtype (classical vs. basal). Patients with classical subtype will receive a standard chemotherapy (mFOLFIRINOX) and patients with basal subtype will receive an alternative standard therapy (gemcitabine/nab-paclitaxel).

NCT#: NCT04683315

Study PI:
Dr. Kathleen Christians

Clinical Research Coordinator:
Lauren Schmitz
Phone: 414-805-5175

Key Inclusion:

Eligibility for Treatment consent:

- ECOG performance status < 2
- Histologically confirmed adenocarcinoma. Biopsy must have been completed prior to start of treatment
- Clinical stage consistent with resectable or borderline resectable or locally advanced type A adenocarcinoma of the pancreas, based on CT or MRI findings
- Adequate organ and bone marrow function, as defined by: total leukocytes >3 x103/μL; ANC >1.5x 103/μL; HgB >9 g/dL; platelets >100 x 10e3/μL; creatinine clearance >60 mL/min or creatinine <1.5 mg/dL; bilirubin < 2 mg/dL; AST/SGOT & ALT/SGPT <3 x ULN

Key Exclusion:

- Received chemotherapy and/or radiation within three years prior to study enrollment
- Previous history of another malignancy w/in 3 years of study (other than cured basal or squamous cell carcinoma and other in situ carcinomas that were completely treated or localized prostate cancer with normal prostate specific antigen)

Clinical Trial Name: Promoting CT Engagement for Pancreatic Cancer With App (PROCLAIM)

Study Design: To develop a culturally tailored informational mobile application and test whether it will increase participation among Black pancreatic cancer subjects in clinical trial discussions with their care team. This project aims to identify and address barriers to enrollment of Black subjects in pancreatic cancer clinical trials using a culturally informed mobile health application to promote participation.

NCT#: NCT06252545

Study PI:
Dr. Ugwuji Maduekwe

Clinical Research Coordinator:
Elizabeth Jeanes
Phone: 414-955-6806

Key Inclusion:

- Participants must meet the following inclusion criteria in order to participate in the mobile health application randomized clinical trial component of the study:
  - Informed consent obtained to participate in the study
  - 18 years or older
  - English speaking
  - Able and willing to participate in the trial
  - Newly diagnosed or progressive pancreatic cancer
  - Have access to a mobile device
  - Identify as Black or African American

Key Exclusion:

- Inability to read and speak English
- Dementia altered mental status, or any psychiatric condition that would prohibit understanding or rendering of informed consent as determined by the study physician.
- Active participation in a therapeutic clinical trial

Clinical Trial Name: Molecular Profile-related Individualized Targeted Therapy in Resected Pancreatic Cancer with High-Risk of Cancer Recurrence (PROTECT-PANC)

Study Design: This is a prospective, open-label therapeutic interventional investigation designed to interrogate the efficacy and safety of individualized matched therapies in patients with pancreatic cancer at high risk of disease recurrence post-surgery.

NCT#: NCT06228599

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Dawn Carini
Phone: 414-805-0789

Key Inclusion:

- Pathologically confirmed pancreatic cancer (excluding neuroendocrine histology).
- Pancreatic tumor is surgically removed and
  - Patient has received multimodal therapy (neoadjuvant, sandwich or adjuvant chemotherapy ± radiation) or
  - Patient is ineligible for or refuses multimodal therapy
- Patient has one of the following:
  - Post-surgical cancer antigen (CA) 19-9 elevation (> 35 U/mL at least 6 weeks post-surgical resection) in the setting of bilirubin < 2 mg/dL (unless bilirubin elevation is consistent with Gilbert's syndrome) OR
  - High-risk pathological features, defined as positive surgical margin or lymph node involvement in cancer.
- Patient has no definitive measurable disease recurrence or metastatic disease at the time of first post-surgical imaging (in those with high-risk pathological features) or within four weeks of elevated CA 19-9 value as evidenced by appropriate imaging
- Laboratory values:
  - Absolute neutrophil count (ANC) ≥ 1.0 × 109/L
  - Platelet count ≥ 75,000/mm^3 (125 × 109/L)
  - Hemoglobin (Hgb) ≥ 8 g/dL
  - aspartate aminotransferase (AST) serum glutamic-oxaloacetic transaminase (SGOT), alanine transaminase (ALT) serum glutamate-pyruvate transaminase (SGPT) ≤ 5 × upper limit of normal range (ULN)
  - ECOG Performance Status < 3
  - At the time of treatment, patient should be off other anti-tumor agents for at least five half-lives of the agent or three weeks from the last day of treatment, whichever is shorter
  - Patient must be presented at the Molecular Tumor Board (MTB) and agree to receive the MTB-recommended therapy
  - Key Exclusion:
  - CA 19-9 non-producers, unless high-risk pathological features present.
  - Receiving concomitant investigational agent(s) for pancreatic ductal adenocarcinoma (PDAC)
  - Radiographic evidence of metastatic disease
  - Inability to ingest study drugs by mouth
  - Diarrheal bowel movements > 6 per day postoperatively on maximal medical therapy
  - Patient has active, untreated, or uncontrolled bacterial, viral, or fungal infection(s) requiring systemic intravenous therapy
  - Patient has undergone or planned major surgery other than diagnostic surgery (i.e., surgery done to obtain a biopsy for diagnosis without removal of an organ) within four weeks prior to Day 1 of study therapy
  - Uncontrolled concurrent illness, including, but not limited to, unstable angina pectoris, uncontrolled and clinically significant cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements

LOCALLY ADVANCED

Clinical Trial Name: PurIST Classification-Guided Adaptive Neoadjuvant Chemotherapy by RNA Expression Profiling of EUS SAmples Study (PANCREAS)

Study Design: This is an open-label, single arm, phase II study in patients with resectable and borderline resectable pancreatic cancer. The study intervention involves molecular profiling Purity Independent Subtyping of Tumors (PurIST) subtyping of pretreatment Endoscopic Ultrasound Fine Needle Aspiration (EUS/FNA) samples to determine pancreatic cancer subtype. Neoadjuvant therapy is directed based on the molecular subtype (classical vs. basal). Patients with classical subtype will receive a standard chemotherapy (mFOLFIRINOX) and patients with basal subtype will receive an alternative standard therapy (gemcitabine/nab-paclitaxel).

NCT#: NCT04683315

Study PI:
Dr. Kathleen Christians

Clinical Research Coordinator:
Lauren Schmitz
Phone: 414-805-5175

Key Inclusion:

Eligibility for Treatment consent:

- ECOG performance status < 2
- Histologically confirmed adenocarcinoma. Biopsy must have been completed prior to start of treatment
- Clinical stage consistent with resectable or borderline resectable or locally advanced type A adenocarcinoma of the pancreas, based on CT or MRI findings
- Adequate organ and bone marrow function, as defined by: total leukocytes >3 x103/µL; ANC >1.5x 103/µL; HgB >9 g/dL; platelets >100 x 10e3/µL; creatinine clearance >60 mL/min or creatinine <1.5 mg/dL; bilirubin < 2 mg/dL; AST/SGOT & ALT/SGPT <3 x ULN

Key Exclusion:

- Received chemotherapy and/or radiation within three years prior to study enrollment
- Previous history of another malignancy w/in 3 years of study (other than cured basal or squamous cell carcinoma and other in situ carcinomas that were completely treated or localized prostate cancer with normal prostate specific antigen)

Clinical Trial Name: Testing Higher Dose Radiation Therapy for Locally Advanced Pancreatic Cancer (NRG-GI011)

Study Design: This phase III trial compares the effect of dose-escalated radiation therapy to usual care in patients with locally advanced unresectable pancreatic ductal adenocarcinoma who have received an initial 4-6 months of chemotherapy. Usual care options include additional chemotherapy, observation, or standard lower-dose radiation therapy. These treatments may delay tumor growth but have not been shown to improve survival. Radiation therapy uses high energy X-rays to kill cancer cells and shrink tumors. Dose-escalated radiation therapy involves the precise delivery of higher doses to the tumor, often over a shorter period of time. This trial assesses whether using dose-escalated radiation therapy can prolong survival.

NCT#: NCT06958328

Study PI:
Dr. William Hall

Clinical Research Coordinator:
Lauren Schmitz
Phone: 414-805-5175

Key Inclusion:

- At time of enrollment, the patient must have received 4-6 months of active chemotherapy with FOLFIRINOX or NALIRIFOX or gemcitabine/nab-paclitaxel. Patients are permitted to receive more than 1 type of chemotherapy for toxicity reasons, but not for disease progression. "Active chemotherapy" refers to time on chemotherapy not counting treatment breaks (i.e. if a patient had 1 month of chemotherapy followed by 1 month break, this would count as 1 month chemotherapy). Study registration must occur within 45 days of last day of chemotherapy cycle
- BASELINE PRE-ENTRY CHEMOTHERAPY REQUIREMENTS:
- Pathologically (histologically or cytologically) proven diagnosis of pancreatic ductal adenocarcinoma
- Locally advanced unresectable disease (as defined per the National Comprehensive Cancer Network [NCCN] guidelines and institutional tumor board review)
- Patients must have baseline pre-chemotherapy scans for staging. Options include: CT chest/abdomen/pelvis, CT chest/MRI abdomen/pelvis, CT chest/CT pelvis/MRI abdomen, or PET/CT performed prior to enrollment
- Age ≥ 18 years
- Performance status Eastern Cooperative Oncology Group (ECOG) 0-2
- Required initial laboratory values:

All laboratory values must be obtained any time prior to initiation of chemotherapy up to 30 days post initiation of chemotherapy

- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 3 x upper limit of normal (ULN)
- BASELINE CA19-9 AND BILIRUBIN REQUIREMENTS: The purpose is to obtain a baseline CA19-9 in the setting of a normal (or close to normal) bilirubin, since serologic response by serial CA19-9 measurements is part of post-chemotherapy eligibility criteria
    - If baseline CA19-9 > 37 U/mL the concurrent bilirubin must be ≤ 1.5 x ULN. (Note: if the bilirubin is not ≤ 1.5 x ULN both the CA19-9 and concurrent bilirubin can be repeated until bilirubin is ≤ 1.5 x ULN, as long as done within specified timeframe [up to 30 days post chemotherapy initiation])
    - If baseline CA19-9 U/mL ≤ 37, there are no restrictions on the required concurrent bilirubin level, and this can be the accepted baseline value
        - Prior radiation treatment
- Has the patient had prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields
- Prior non-overlapping radiation (e.g., breast, head and neck, extremity) is permitted

NRG-GI011 (Continued)	• If uncertain about prior overlap, please contact the study principal investigator, Dr. Nina Sanford ◦ POST PRE-ENTRY CHEMOTHERAPY REQUIREMENTS: ◦ If baseline CA19-9 is elevated (defined as > 37 u/mL) the post-pre-entry chemotherapy CA19-9 must be less than 37 u/mL or a 50% decline from pre-chemotherapy level with absolute value less than 100u/mL ◦ If baseline CA19-9 is not elevated (defined as ≤ 37 u/mL) the post-pre-entry chemotherapy CA19-9 must remain ≤ 37 u/mL ◦ No active duodenal or gastric ulcers ◦ No direct tumor invasion of the bowel or stomach ◦ Restaging scans showing at least stable disease (no progression). Options for scans include: CT chest/abdomen/pelvis, CT chest/MRI abdomen/pelvis, or CT chest/CT pelvis/MRI abdomen, or PET/CT performed prior to enrollment, with restaging CT showing at least stable disease ◦ Not pregnant and not nursing ◦ No cardiac condition that was the primary reason for hospitalization in the last 6 months ◦ New York Heart Association Functional Classification II or better (NYHA Functional Classification III/IV are not eligible) (Note: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification.) ◦ HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial

Clinical Trial Name: Molecular Profile-related Individualized Targeted Therapy in Resected Pancreatic Cancer with High-Risk of Cancer Recurrence (PROTECT-PANC)

Study Design: This is a prospective, open-label therapeutic interventional investigation designed to interrogate the efficacy and safety of individualized matched therapies in patients with pancreatic cancer at high risk of disease recurrence post-surgery.

NCT#: NCT06228599

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Dawn Carini
Phone: 414-805-0789

Key Inclusion:

- Pathologically confirmed pancreatic cancer (excluding neuroendocrine histology).
- Pancreatic tumor is surgically removed and
  - Patient has received multimodal therapy (neoadjuvant, sandwich or adjuvant chemotherapy ± radiation) or
  - Patient is ineligible for or refuses multimodal therapy
- Patient has one of the following:
  - Post-surgical cancer antigen (CA) 19-9 elevation (> 35 U/mL at least 6 weeks post-surgical resection) in the setting of bilirubin < 2 mg/dL (unless bilirubin elevation is consistent with Gilbert's syndrome) OR
  - High-risk pathological features, defined as positive surgical margin or lymph node involvement in cancer.
- Patient has no definitive measurable disease recurrence or metastatic disease at the time of first post-surgical imaging (in those with high-risk pathological features) or within four weeks of elevated CA 19-9 value as evidenced by appropriate imaging
- Laboratory values:
  - Absolute neutrophil count (ANC) ≥ 1.0 × 109/L
  - Platelet count ≥ 75,000/mm^3 (125 × 109/L)
  - Hemoglobin (Hgb) ≥ 8 g/dL
  - aspartate aminotransferase (AST) serum glutamic-oxaloacetic transaminase (SGOT), alanine transaminase (ALT) serum glutamate-pyruvate transaminase (SGPT) ≤ 5 × upper limit of normal range (ULN)
  - ECOG Performance Status < 3
  - At the time of treatment, patient should be off other anti-tumor agents for at least five half-lives of the agent or three weeks from the last day of treatment, whichever is shorter
  - Patient must be presented at the Molecular Tumor Board (MTB) and agree to receive the MTB-recommended therapy

Key Exclusion:

- CA 19-9 non-producers, unless high-risk pathological features present.
- Receiving concomitant investigational agent(s) for pancreatic ductal adenocarcinoma (PDAC)
- Radiographic evidence of metastatic disease
- Inability to ingest study drugs by mouth
- Diarrheal bowel movements > 6 per day postoperatively on maximal medical therapy
- Patient has active, untreated, or uncontrolled bacterial, viral, or fungal infection(s) requiring systemic intravenous therapy
- Patient has undergone or planned major surgery other than diagnostic surgery (i.e., surgery done to obtain a biopsy for diagnosis without removal of an organ) within four weeks prior to Day 1 of study therapy
- Uncontrolled concurrent illness, including, but not limited to, unstable angina pectoris, uncontrolled and clinically significant cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements

METASTATIC

PHASE I/II STUDIES

Clinical Trial Name: Phase I Study, a master protocol to investigate TCR-Engineered T cells recognizing KRAS mutations in adult subjects with Unresectable, Advanced, and/or Metastatic Solid Tumors (NEOGENE-NT-112-301)

Study Design: This is a Phase I, open-label, Phase I, Multi-Center Master Protocol to evaluate the safety and preliminary Anti-Tumor activity of TCR-Engineered T cells (KRAS TCRTs) recognizing KRAS mutations in adult subjects with Unresectable, Advanced, and/or Metastatic Solid Tumors.

NCT#: NCT06218914

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Kathryn Wendorf, RN
Phone: 414-805-5153

Key Inclusion:

- Age ≥18 years
- Diagnosed with NSCLC, Colorectal adenocarcinoma, Pancreatic adenocarcinoma, Endometrial Cancer or any other solid tumor
- Tumors must harbor a KRAS G12D variant mutation and subject must be HLA-C*08:02 positive, HLA-A*11:01 or HLA-A*11:02 positive in at least one allele
- Subject has advanced solid cancer, defined as unresectable, advanced, and/or metastatic disease (Stage III or IV) after at least 1 line of approved systemic standard of care (SOC) treatment regimen and for which there are no available curative treatment options.
- Presence of at least 1 measurable lesion per RECIST v1.1
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1 at the time of enrollment

Key Exclusion:

- Any other primary malignancy within the 3 years prior to enrollment (except for non-melanoma skin cancer, carcinoma in situ (eg, cervix, bladder, breast) or low-grade prostate cancer
- Known, active primary central nervous system (CNS) malignancy
- History of prior adoptive cell and gene therapy, allogeneic stem cell transplant or solid organ transplantation.
- History of stroke or transient ischemic attack within the 12 months prior to enrollment.
- History of clinically significant cardiac disease within the 6 months prior to enrollment or heart failure at any time prior to enrollment.
- Systemic therapy within at least 2 weeks or 3 half-lives, whichever is shorter, prior to enrollment.
- Any form of primary immunodeficiency.
- Active immune-mediated disease requiring systemic steroids or other immunosuppressive treatment (except if related to prior checkpoint inhibitor therapy)
- Female of childbearing potential who is lactating or breast feeding at the time of enrollment
- Prior treatment with pan-KRAS or KRAS G12D targeting agents unless presence of KRAS G12D mutation is confirmed after the completion of treatment with pan-KRAS or KRAS G12D targeting agents.

Clinical Trial Name: A Phase I/Ib Study of ASP2138 in Participants with Metastatic or Locally Advanced Unresectable Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma or Metastatic Pancreatic Adenocarcinoma (ASTELLAS).

Study Design: A Phase I/Ib Study of ASP2138 in Participants with Metastatic or Locally Advanced Unresectable Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma or Metastatic Pancreatic Adenocarcinoma Whose Tumors Have Claudin (CLDN) 18.2 Expression.

NCT#: NCT05365581

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Morgan Ward
Phone: 414-805-6345

Key Inclusion:

- Tumor sample is positive for claudin (CLDN)18.2 expression by central immunohistochemistry (IHC) testing.
- Radiographically-confirmed, locally advanced, unresectable or metastatic disease within 28 days prior to the first dose of study intervention
- Measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 within 28 days prior to the first dose of study intervention. For participant with only 1 measurable lesion and prior radiotherapy, the lesion must be outside the field of prior radiotherapy or must have documented progression following radiation therapy.
- QT interval by Fredericia (QTcF) =< 470 msec.
- Participant has ECOG performance status of 0 or 1.
- Disease Specific Criteria: Pancreatic Cancer
  - Participant has histologically or cytologically confirmed pancreatic adenocarcinoma.
  - Participant with pancreatic adenocarcinoma who has progressed, is intolerant, has refused, or for whom there is no standard approved therapies that impart significant clinical (no limit to the number of prior treatment regimens).

Key Exclusion:

- Prior severe allergic reaction or intolerance to known ingredients of ASP2138 or other antibodies, including humanized or chimeric antibodies.
- Received systemic immunosuppressive therapy, including systemic corticosteroids 14 days prior to first dose of study intervention.
- Complete gastric outlet syndrome or a partial gastric outlet syndrome with persistent/recurrent vomiting.
- Gastric bleeding and/or untreated gastric ulcers that exclude the participant from participation.
- Symptomatic CNS metastases or participant has evidence of unstable CNS metastases even if asymptomatic.
- Known HIV infection.
- Participant is known to have active hepatitis B (positive hepatitis B surface antigen [HBsAg]) or hepatitis C infection. Testing is required for known history of these infections or as mandated by local requirements.
- Negative for HBsAg, but hepatitis B core antibody (HBc Ab) positive, a hepatitis B virus (HBV) deoxyribonucleic acid (DNA) test will be performed and if positive the participant will be excluded.
- Positive hepatitis C virus (HCV) serology, but negative HCV ribonucleic acid (RNA) test results are eligible.
- Treated for HCV with undetectable viral load results are eligible.
- Within 6 months prior to first dose of study intervention any of the following: unstable angina, myocardial infarction, ventricular arrhythmia requiring intervention or hospitalization for heart failure.
- Active infection requiring systemic therapy that has not completely resolved within 7 days prior to the start of study intervention.
- Active autoimmune disease that has required systemic immunosuppressive treatment within the past 1 month prior to the start of study intervention.
- Major surgical procedure 28 days before start of study intervention and has not fully recovered. · Received radiotherapy for locally advanced unresectable or metastatic gastric or GEJ or metastatic pancreatic adenocarcinoma 14 days prior to start of study intervention and has NOT recovered from any related toxicity.

ASTELLAS (Continued)	• Received an CLDN18.2-targeted investigational agent (e.g., zolbetuximab or chimeric antigen receptor CLDN18.2-specific T cells) prior to first dose of study intervention administration is not eligible for dose escalation cohorts. However, a participant who has received an CLDN18.2-targeted investigational agent greater than 28 days or 5 half-lives (whichever is longer) prior to first dose study intervention administration is eligible for dose expansion cohorts only, except for participants who have experienced Grade >= 3 gastrointestinal (GI) toxicity after receiving an CLDN18.2-targeted investigational agent. • History or complication of interstitial lung disease.

Clinical Trial Name: Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy for Patients (IIT-GEORGE-I-PREDICT)

Study Design: The purpose of this study is to learn more about personalized cancer therapy, including response to treatment and its side effects. Personalized cancer therapy is the practice of making decisions about what kind of treatment patients should receive based on the characteristics of their tumor.

NCT#: NCT05674825

Study PI:
Dr. Hui-Zi Chen

Clinical Research Coordinator:
Paola Gonzalez Quevedo

Phone: 414-805-2674

Key Inclusion:

- Patient with aggressive solid malignancy must meet at least one of the following:
  - Malignancy with ≥30% two-year cancer-associated mortality as estimated by the treating oncologist and one of the study investigators and/or, where appropriate, according to accepted data sets in the field (e.g., NCDB). Diseases include but are not limited to: ampullary carcinoma, appendiceal cancer, colorectal cancer (CRC), extrahepatic cholangiocarcinoma (EHCC), esophageal adenocarcinoma, gallbladder cancer (GBCA) gastric adenocarcinoma, head and neck cancer, hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (IHCC), melanoma, non-KIT gastrointestinal stromal tumor (GIST), non-small cell lung cancer (NSCLC), ovarian cancer, pancreatic ductal adenocarcinoma (PDAC), sarcoma (high-grade), small bowel adenocarcinoma (including duodenal), triple-negative breast cancer (TNBC), urothelial cancer
  - Refused standard therapies, OR
  - Cancer of unknown primary or a rare tumor (i.e., fewer than 4 cases per 100,000 per year) with no approved therapies.
- Patient with aggressive solid malignancy irrespective of two-year mortality who, in the opinion of the investigator, has no treatment option expected to yield significant clinical benefit.
- Patient must have at least one of the following for a diagnosis/disease status:
  - Unresectable disease, as determined by a disease-appropriate multidisciplinary tumor board.
  - Medically unfit for surgical resection but with an expected survival of > three months.
  - Localized disease and are eligible for neoadjuvant treatment.
  - Metastatic disease.
  - Disease where no conventional therapy leads to a survival benefit > six months in the respective cohort and line of therapy for which the patient is otherwise eligible.
- Patient is either:
  - Treatment naïve for their newly diagnosed malignancy (for enrollment to Groups 1 or 2), or
  - Status post one or more systemic therapy regimens, whether matched or unmatched (for enrollment to Group 3). Note: There are no limitations on the number of prior local therapies.
- Patient must have measurable disease for malignancy: defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded for non-nodal lesions and short axis for nodal lesions) as ≥20 mm with conventional techniques or as ≥10 mm with spiral CT scan, positron emission tomography (PET) -CT, MRI, or calipers by clinical exam.
- ECOG:0-2

IIT-GEORGE-I-PREDICT (Continued)	• New York Heart Association (NYHA) Functional Classification I-II
	• Adequate organ and marrow function as defined below:
	  ◦ Absolute neutrophil count ≥ 1.0 x 109/L
	  ◦ Platelet count ≥ 75 x 109/L § Total bilirubin ≤ 2.0 x institution's upper limit of normal (ULN)
	  ◦ Patients without underlying liver disease: alanine transaminase (ALT) and aspartate aminotransferase (AST) ≤ 3 x institutional ULN
	  ◦ Serum creatinine ≤ 2.0 x institution's ULN or 24-hour creatinine clearance ≥ 30 ml/min
	•
	• At the time of treatment, patient should be off other anti-tumor agents for at least five half-lives of the agent or two weeks from the last day of treatment, whichever is shorter to enroll in Group 3. Patient must not have been treated with anti-tumor agents to enroll in Group 1 or Group 2. Patient must be off prior antibody therapy for at least three half-lives before starting treatment.
	• If actionable or appropriate molecular profiling has not already been performed, patient must have or provide evaluable tissue and/or blood for molecular profiling. This could be obtained during the standard of care tumor diagnosis or tumor staging evaluation. Tissue and/or blood is to be procured based on clinical discretion and discussion with the patient.
	• Patients presented at Molecular Tumor Board (MTB) up to two weeks prior to signing consent are eligible to be treated on study based on the MTB recommendations and do not need to be represented at MTB prior to starting therapy on trial (unless six months elapsed between consent and start of study treatment).
	Key Exclusion:
	• Two oncologists disagree on prognosis or resectability.
	• Severe or uncontrolled medical disorder that would, in the investigator's opinion, confound study analyses of treatment response (i.e., uncontrolled diabetes, chronic renal disease, chronic pulmonary disease or active, uncontrolled infection, psychiatric illness/social situations that would limit compliance with study requirements).
	• Is pregnant or breastfeeding or any patient with childbearing potential not using adequate pregnancy prevention. Whole brain radiation or stereotactic radiotherapy to CNS metastases within 14 days prior to start of study treatment.

Clinical Trial Name: COLUMBIA-S9513-CHEMO4METPANC

Study Design: A Phase II Study With Combination Chemotherapy (Gemcitabine and Nab-Paclitaxel), Chemokine (C-X-C) Motif Receptor 4 Inhibitor (BL-8040), and Immune Checkpoint Blockade (Cemiplimab) in METastatic Treatment naïve PANCreas Adenocarcinoma

NCT#: NCT04543071

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Sophia Davis
Phone: 414-805-5278

Key Inclusion:

- Histological or pathological confirmation of metastatic pancreas adenocarcinoma
  - Cytologic or histologic proof of pancreas adenocarcinoma needs to be verified by the treating institution pathologist, either from the initial diagnostic biopsy or from the required pre-treatment biopsy, prior to initiation of any study-related therapy.
  - Pathologic confirmation of metastatic (stage IV) disease (unresectable) on research pretreatment biopsy is required prior to initiation of therapy.
  - Patients with endocrine or acinar pancreatic carcinoma are not eligible for the study.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Age ≥18 years
- Adequate hematological and end-organ function (test results from within 14 days prior to initiation of study treatment):
  - Absolute Neutrophil Count (ANC) ≥ 1.5 x 109/L without granulocyte colony-stimulating factor support
  - White Blood Cell Count (WBC) count ≥ 2.5 x 109 /L (2500/uL)
  - Lymphocyte count ≥ 0.5 x 109/L (500/uL)
  - Platelet count ≥ 100 x 109/L (100,000/uL) without transfusion
  - Hgb ≥ 9.0 g/dL
  - Aspartate aminotransferase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) ≤ 2.5X upper limit of normal (ULN), unless elevated secondary to biliary obstruction from the pancreas mass and amenable to decompression prior to initiation of therapy
  - Serum total bilirubin ≤ 1.5X ULN, unless in patients with known Gilbert disease (≤ 3X ULN), or unless elevated secondary to biliary obstruction from the pancreas mass and amenable to decompression prior to administration of investigational therapy
  - Albumin ≥ 3.5 g/dL
  - Creatinine within ULN or calculated creatinine clearance (CrCl) >50 mL/min using the Cockcroft-Gault formula
  - International normalized ratio (INR) and activated partial thromboplastin time (aPTT) ≤ 1.5X ULN, except for those on stable anticoagulation for at least two weeks
- Measurable disease according to Immune Modified (IM)-RECIST and tumor accessible for fresh biopsy
- Negative pregnancy test: Women of child-bearing potential must have a negative serum pregnancy test at screening and must agree to use an effective form of contraception from the time of the negative pregnancy test until a minimum of 3 months after the last dose of study drug. Effective forms of contraception include abstinence, hormonal contraceptive (injectable or implantable) in conjunction with a barrier method. Women of non-child-bearing potential must have been postmenopausal for ≥ 1 year or surgically sterile.
- Birth control agreement: Fertile men must agree to use an effective method of birth control with female partners of childbearing potential (condoms plus an additional contraceptive method such as an injectable or implantable hormonal contraceptive) during the study and for up to 3 months after the last dose of study drug.
- Informed consent: Participants must be willing and able to provide written informed consent prior to any study-related procedures and to comply with all study requirements.
- Ability to comply: Participants must be able to comply with the study protocol, according to the investigator's judgement.
- DVT testing Participants must have undergone lower extremity dopplers to rule out deep venous thrombosis (DVT) within the screening period, and undergo therapeutic anticoagulation if evidence of DVT is identified.

Columbia-CHEMO4METPANC (Continued)	• Anticoagulation treatment Subjects who are stable on full-dose anticoagulation medication for at least 2 weeks are considered eligible. However, subjects who have an increased clot burden on full-dose anticoagulation, such as central pulmonary embolism, or peripheral pulmonary embolism, and DVT within the extremities will be considered eligible only with the approval of the Principal Investigator. ***Key Exclusion:*** • Prior systemic therapy for PDAC: Participants may not have had systemic chemotherapy, investigational therapy, or treatment with T-cell co-stimulating or immune check point blockade therapies (including anti-CTLA-4, anti PD-1, and anti PD-L1 therapeutic antibodies) prior to initiation of study treatment. • Prior radiation therapy for PDAC Participants may not have had radiation therapy to within two weeks prior to initiation of study treatment. Participants may not have had previous radiotherapy to the primary pancreas lesion or a metastatic site except for palliation for pain. Participants who receive radiation to 25% or more of the bone marrow will be excluded. • Prior surgery for PDAC Participants may not have had surgical resection of PDAC prior to initiation of study treatment • Patients currently receiving any other investigational agents • Adverse events from prior anti-cancer therapy that have not resolved to Grade ≤ 1 or better, with the exception of alopecia of any grade and Grade ≤ 2 peripheral neuropathy • Concomitant treatment with other anti-neoplastic agents (hormone therapy acceptable) • Uncontrolled pleural effusion, pericardial effusion, or ascites. Subjects who required drainage within the four weeks prior or require pleural, pericardial, or peritoneal catheters for drainage are ineligible. • Uncontrolled tumor-related pain Patients requiring narcotic pain medication must be on a stable regimen for at least two weeks prior to study entry. • History of leptomeningeal or brain/ Central Nervous System (CNS) metastases • Uncontrolled hypercalcemia (ionized calcium > 1.5 mmol/L, calcium > 12 mg/dL, or corrected serum calcium > upper limit of normal) or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy. • Recent major surgery or significant traumatic injury Participants may not have undergone major surgery or experienced significant traumatic injury within 14 days prior to initiating study treatment, or be recovering from procedure related adverse events of > Grade 1. • Active or history of autoimmune disease or immune deficiency Includes, but is not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, or multiple sclerosis, with the following exceptions: ◦ Patients with a history of autoimmune-related hypothyroidism who are on stable thyroid-replacement hormone for the past three months are eligible for the study. ◦ Patients with controlled Type 1 diabetes mellitus who are on a stable insulin regimen for the past month are eligible for the study. ◦ Patients with eczema, psoriasis, lichen simplex chronicus, or vitiligo with dermatologic manifestations only (e.g., patients with psoriatic arthritis are excluded) are eligible for the study provided all of following conditions are met: ▪ Rash must cover <10% of body surface area; ▪ Disease is well-controlled at baseline and requires only low-potency topical corticosteroids; ▪ No occurrence of acute exacerbations of the underlying condition requiring psoralen plus ultraviolet A radiation, methotrexate, retinoids, biologic agents, oral calcineurin inhibitors, or high-potency or oral corticosteroids within the previous 12 months. • History of idiopathic pulmonary fibrosis, interstitial lung disease, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography scan (history of radiation pneumonitis or fibrosis in the radiation field is permitted). • Positive for HIV at screening or any time prior to screening Patients without prior positive HIV test result will undergo an HIV test at screening, unless not permitted under local regulations.

Columbia-CHEMO4METPANC (Continued)	• Hepatitis B virus (HBV) infection (chronic or acute) Defined as having a positive hepatitis B surface antigen (HBsAg) test at screening. Patients with a past or resolved HBV infection, defined as having a negative HBsAg test and a positive total hepatitis B core antibody test at screening, are eligible for the study. • Active hepatitis C virus (HCV) infection: Defined as positive HCV antibody test followed by a positive HCV RNA test at screening. • The HCV RNA test will be performed only for patients who have a positive HCV antibody test. • Known clinically significant liver disease, including alcoholic hepatitis, cirrhosis, fatty liver disease, and inherited liver disease. • Active tuberculosis • Infection: Patients may not have had a severe infection requiring antibiotic treatment within the two weeks prior to initiation of study treatment. This includes, but is not limited to, hospitalization for complications of infection, bacteremia, or severe pneumonia. However, patients who were admitted for biliary tract infection due to bile duct obstruction at time of diagnosis must have a functioning biliary stent (as evidenced by declining total bilirubin and ≤ 2X ULN) and resolved infection (defined by normalization of elevated white blood cell count, absence of signs of infection) and completion of an antibiotic course (at least a seven-day course) prior to initiation of therapy. Patients receiving prophylactic antibiotics (e.g., to prevent a urinary tract infection or chronic obstructive pulmonary disease exacerbation) are eligible for the study. • Significant cardiovascular disease: Patient may not have significant cardiovascular disease (such as New York Heart Association Class II or greater cardiac disease, myocardial infarction, or cerebrovascular accident) within 12 months prior to initiation of study treatment, seizure disorder, uncontrolled hypertension, or unstable arrhythmia or unstable angina within 3 months prior to initiation of study treatment. • Left ventricular ejection fraction below institutional lower limit of normal or below 50%, whichever is lower. • Baseline QTcF ≥ 450 ms (males) or ≥ 470 ms (females) • Grade ≥ 3 hemorrhage or bleeding event within 28 days prior to initiation of study treatment • Prior autologous stem cell, allogeneic stem cell, or solid organ transplantation • History of other malignancy Patient may not have a history of malignancy other than PDAC within two years prior to screening, with the exception of those with a negligible risk of metastasis or death (e.g., 5- year overall survival of > 90%), such as adequately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localized prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer. • Recent vaccination: Patients may not have been treated with a live, attenuated vaccine within four weeks prior to initiation of study treatment, or anticipate the need for such a vaccine during treatment with cemiplimab or within five months after the last dose of cemiplimab. • History of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins • Known allergy or hypersensitivity to any of the study drug excipients • Recent immunosuppressive treatment: Patients may not have been treated with systemic immunosuppressive medication (including, but not limited to, corticosteroids, cyclophosphamide, azathioprine, methotrexate, thalidomide, calcineurin inhibitors, and anti-tumor necrosis factor alpha agents) within two weeks prior to initiation of study treatment, or anticipate the need for systemic immunosuppressive medication during the course of the study, with the following exceptions: • Patients who received a one-time pulse dose of systemic immunosuppressant medication are eligible for the study after approval from the Principal Investigator. • Pregnancy: Pregnant women are excluded from this study because there is an unknown, but potential risk for adverse events to the fetus. Breastfeeding should be discontinued prior to start of treatment because there is an unknown, but potential risk for adverse events in nursing infants secondary to treatment.

Columbia-CHEMO4METPANC (Continued)	• Other contraindicated conditions Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the patient at high risk from treatment complications in the opinion of the treating investigator. • Uncontrolled psoriasis, porphyria, proximal myopathy or neuropathy • Severe depression Subjects hospitalized for depression within the past two years, or who have prior suicidal attempts will be excluded. • Has received transfusions of blood products (including platelets or red blood cells) within 4 weeks prior to study Day 1. • Patients who received mineralocorticoids (e.g., fludrocortisone), corticosteroids for chronic obstructive pulmonary disease or asthma, or low-dose corticosteroids for orthostatic hypotension or adrenal insufficiency are eligible for the study if receiving equivalent to ≤ 10 mg of prednisone daily (10mg prednisone is equivalent to either cortisone - 50mg; hydrocortisone - 40mg; triamcinolone - 8mg; prednisolone - 10mg; methylprednisolone - 8mg; betamethasone - 1.5mg; or dexamethasone - 1.5mg). Patients receiving > 10 mg of prednisone or equivalent per day for greater than five days within 28 days of starting study related therapy are not eligible. Steroids administered prior to gemcitabine and nab-paclitaxel should be administered as per standard institutional guidelines.

Clinical Trial Name: Promoting CT Engagement for Pancreatic Cancer With App (PROCLAIM)

Study Design: To develop a culturally tailored informational mobile application and test whether it will increase participation among Black pancreatic cancer subjects in clinical trial discussions with their care team. This project aims to identify and address barriers to enrollment of Black subjects in pancreatic cancer clinical trials using a culturally informed mobile health application to promote participation.

NCT#: NCT06252545	***Key Inclusion:***
	• Participants must meet the following inclusion criteria in order to participate in communication & education interview component of the study:
	  ◦ Informed consent obtained to participate in the study
	  ◦ 18 years or older
	  ◦ English speaking
	  ◦ Able and willing to participate in a 1-hour interview
	  ◦ History of pancreatic cancer diagnosis
	  ◦ Identify as Black
	Key Exclusion:
	• Inability to read and speak English
	• Dementia altered mental status, or any psychiatric condition that would prohibit understanding or rendering of informed consent as determined by the study physician.

Study PI: Dr. Ugwuji Madeuekwe	
Clinical Research Coordinator: Elizabeth Jeanes **Phone:** 414-955-6806	

Clinical Trial Name: A Study Comparing BMS-986504 in Combination With Nab-paclitaxel and Gemcitabine Versus Placebo in Combination With Nab-paclitaxel and Gemcitabine in Participants With Untreated Metastatic Pancreatic Ductal Adenocarcinoma With Homozygous MTAP Deletion (MountainTAP-30)

Study Design: The purpose of this study is to assess the safety and efficacy of BMS-986504, a selective, MTA-cooperative PRMT5 inhibitor, in combination with Nab-paclitaxel/Gemcitabine (nab-p/gem) versus placebo in combination with nab-p/gem, in participants with untreated metastatic Pancreatic Ductal Adenocarcinoma (PDAC) with homozygous methylthioadenosine phosphorylase (MTAP) deletion.

NCT#: NCT07076121

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Dawn Carini
Phone: 414-805-0789

Key Inclusion:

- Histologically or cytologically confirmed diagnosis of metastatic pancreatic ductal adenocarcinoma (PDAC).
- Evidence of homozygous methylthioadenosine phosphorylase (MTAP) deletion or MTAP loss detected in tumor tissue.
- Metastatic disease with at least 1 measurable lesion as per Response Evaluation Criteria in Solid Tumors version v1.1 (RECIST v1.1).
- Participants must not have received any systemic anticancer treatments in the metastatic setting.
- If clinically indicated and as per investigator discretion, participants may receive up to 1 cycle of Nab-paclitaxel/Gemcitabine (nab-p/gem) in the metastatic setting and must have not progressed or required discontinuation due to intolerable toxicity.
- Initial cycle of nab-p/gem administered in the metastatic setting must have been completed prior to randomization.

Key Exclusion:

- Concurrent malignancy (present during screening) requiring treatment or history of prior malignancy active within 2 years prior to screening.
- Other protocol-defined Inclusion/Exclusion criteria apply.

PANCREATIC NEUROENDOCRINE

Clinical Trial Name: SWOG-S201 Randomized Phase II/III Trial of First Line Platinum/Etoposide with or without Atezolizumab (NSC#783608) in Patients with Advanced or Metastatic Poorly Differentiated Extrapulmonary Neuroendocrine Carcinomas (NEC)

Study Design: This is a randomized, multi-center phase II/III trial in patients with advanced or metastatic poorly differentiated extrapulmonary neuroendocrine carcinomas (NEC). Patients are randomized to either 4 cycles of Platinum/Etoposide + Atezolizumab + maintenance Atezolizumab for up to 1 year; 4 cycles of Platinum/Etoposide + Atezolizumab + Observation; or 4 cycles Platinum/Etoposide + Observation. The purpose of the study is to compare the different treatment arms and overall survival across the arms.

NCT#: NCT05058651

Study PI:
Dr. Alexandria Phan

Clinical Research Coordinator:
Dawn Carini
Phone: 414-805-0789

Key Inclusion:

- Histologically confirmed extrapulmonary poorly differentiated, neuroendocrine carcinoma (NEC)
- Disease that is unresectable or metastatic and not eligible for definitive therapy as deemed per the treating investigator
- Must have radiologically evaluable disease, measurable or non-measurable, per RECIST 1.1 criteria.
- Participants must have a Zubrod Performance Status of < 2.

Key Exclusion:

- Participants must not have symptomatic central nervous system (CNS) metastases.
- Participants must not have had prior treatment for advanced or metastatic NEC EXCEPT for one cycle of platinum (carboplatin/cisplatin) + etoposide is allowed prior to registration. Other chemotherapy regimens are not allowed.
- Participants must not have had prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, CD137 agonists, anti-CTLA-4 agent, or any other immune checkpoint inhibitors for any neuroendocrine neoplasm. Immune checkpoint inhibitors given for other cancer indications are allowed provided last therapy was given at least 12 months prior to study registration.
- Participants must not have received treatment with systemic immunostimulatory agents including, but not limited to, interferon and interleukin2 [IL-2] within 4 weeks or 5 half-lives of the drug (whichever is longer) prior to registration.