PANCREATIC CANCER

LaBahn Pancreatic Cancer Program
Hope Innovation Discovery Cure

CLINICAL TRIAL PORTFOLIO

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. SOFT Trial - Phase II RCT of IMRT vs SBRT prior to surgery

B. Prior Neoadjuvant Chemotherapy
  I. SOFT Trial - Phase II, RCT of IMRT vs SBRT prior to surgery
  II. COLUMBIA-AAAU4206-AIRPANC- Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in patients with PDAC

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. SOFT Trial - Phase II, RCT of IMRT vs SBRT prior to surgery
  II. PANCREAS Trial – Phase II Trial of Tumor Subtype-directed Neoadjuvant Chemotherapy

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. ASTELLAS-2138-CL-0101- Phase I/Ib, ASP2138 in Adults with Stomach Cancer or Pancreatic Cancer (check for slot availability)
  II. MIRATI 1719-001 - A Phase I/II Multiple Expansion Cohort Trial of MRTX1719 in Patients with Advanced Solid Tumors with Homozygous MTAP Deletion (check for slot availability)
  III. IIT-GEORGE-I-PREDICT- Phase I/II, Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy for Patients

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)
II. HARPOON HPN328-4001: A Phase I/II Open-label, Multicenter, Dose Escalation and Dose Expansion Study of the Safety, Tolerability, and Pharmacokinetics of HPN328 Monotherapy and, HPN328 with Atezolizumab or Ifinatamab Deruxtecan (I-DXd) in Patients with Advanced Cancers Associated with Expression of Delta-like Canonical Notch Ligand 3 (DLL3)

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:
Megan Graham
Phone: 414-805-8921

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:
Megan Graham
Phone: 414-805-8921

Key Inclusion:

Eligibility for screening consent:

- Suspicion of PDAC and plan for endoscopic biopsy or enough archival tissue to be requested from previous screening endoscopic biopsy. Agrees to additional EUS biopsy at the first restaging and tissue collection from surgical specimen

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: Stereotactic Body Radiation Therapy or Conventionally Fractionated Concurrent Chemotherapy and Radiation Therapy Preoperatively for Resectable or Borderline Resectable Pancreatic Adenocarcinoma (SOFT Trial)

Study Design: This study is a prospective, open-label, randomized, parallel, two-arm, phase II clinical trial. Patients meeting the eligibility criteria will be randomized after a minimum of two months of induction chemotherapy. These patients will be required to have no biopsy-proven distant disease on repeat staging studies before randomization. Patients who have radiologically equivocal evidence of distant metastatic disease (small lung nodules, or liver lesions that cannot be definitively characterized, etc.) are also eligible for enrollment. Patients with biopsy-proven metastatic disease are not eligible.

NCT#: NCT03322995

Study PI:
Dr. Kathleen Christians

Clinical Research Coordinator:
Grace Westerman
Phone: 414-805-8986

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: Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in patients with PDAC (COLUMBIA-AAAU4206-AIRPANC)

Study Design: A Phase 2, Open-Label, Multicenter, Randomized Study Evaluating Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in Patients with Advanced PANCreatic Ductal Adenocarcinoma Who Are Candidates for Surgical Resection

NCT#: NCT06048484

Study PI:
Dr. Ben George

Research Coordinator:
Grace Westerman
Phone: 414-805-8986

Key Inclusion:

- Histological or pathological confirmation of pancreatic adenocarcinoma Cytologic or histologic proof of pancreatic ductal adenocarcinoma (PDAC) needs to be verified by the treating institution pathologist. A pathological report from non-treating institutions is sufficient to consent and to initiate investigational therapy if tissue sample is unavailable for evaluation at time of consent or enrollment. However, in such a case, PDAC diagnosis should be confirmed by the treating institution pathologist at a later time.
- Completed 8 cycles of neoadjuvant modified FOLFIRINOX. Omission of oxaliplatin due to adverse events may be allowed in cycles 5-8 with consultation with the principal investigator.
- Patients with surgically resectable PDAC who are considered appropriate to undergo the applicable operation. MCW's criteria of borderline resectable meets this inclusion criteria.
- Eligible to undergo SBRT.
- Measurable disease as per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.
- No prior surgical, systemic, or radiotherapy for PDAC except for mFOLFIRINOX.
- ECOG: 0 or 1.

Clinical Trial Name: Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in patients with PDAC (COLUMBIA-AAAU4206-AIRPANC) Continued	***Key Exclusion:*** • Prior treatment with T-cell co-stimulating or immune checkpoint blockade therapies, including but not limited to anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies. • Uncontrolled pleural effusion, pericardial effusion, or ascites. • Uncontrolled hypercalcemia (ionized calcium > 1.5 mmol/L, calcium > 12 mg/dL, or corrected serum calcium > ULN) or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy. • Active or history of autoimmune disease or immune deficiency, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease (Crohn's disease or ulcerative colitis), antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, or multiple sclerosis (some exceptions permissible as outlined per protocol). • 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 CT scan. • History of radiation pneumonitis in the radiation field (fibrosis) is permitted. • Positive HIV test at screening or at any time prior to screening. • Active hepatitis B virus (HBV) infection (chronic or acute), defined as having a positive hepatitis B surface antigen (HBsAg) test at screening. • Active hepatitis C virus (HCV) infection, defined as having a 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. • History of allergy or hypersensitivity to oxaliplatin, irinotecan, leucovorin, fluorouracil, pegfilgrastim, or any excipients • History of Gilbert's disease or known genotype UGT1A1 *28/*28.

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	***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)

Study PI: Dr. Mandana Kamgar	
Clinical Research Coordinator: Dawn Carini **Phone:** 414-805-0789	

Clinical Trial Name: Molecular Profile-related Individualized Targeted Therapy in Resected Pancreatic Cancer with High-Risk of Cancer Recurrence (PROTECT-PANC) Continued	◦ 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: Stereotactic Body Radiation Therapy or Conventionally Fractionated Concurrent Chemotherapy and Radiation Therapy Preoperatively for Resectable or Borderline Resectable Pancreatic Adenocarcinoma (SOFT Trial)

Study Design: This study is a prospective, open-label, randomized, parallel, two-arm, phase II clinical trial. Patients meeting the eligibility criteria will be randomized after a minimum of two months of induction chemotherapy. These patients will be required to have no biopsy-proven distant disease on repeat staging studies before randomization. Patients who have radiologically equivocal evidence of distant metastatic disease (small lung nodules, or liver lesions that cannot be definitively characterized, etc.) are also eligible for enrollment. Patients with biopsy-proven metastatic disease are not eligible.

NCT#: NCT03322995

Study PI:
Dr. Kathleen Christians

Clinical Research Coordinator:
Grace Westerman
Phone: 414-805-8986

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:
Megan Graham
Phone: 414-805-8921

Key Inclusion:

Eligibility for screening consent:

- Suspicion of PDAC and plan for endoscopic biopsy or enough archival tissue to be requested from previous screening endoscopic biopsy. Agrees to additional EUS biopsy at the first restaging and tissue collection from surgical specimen

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

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

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

A Phase 1/1b Study of ASP2138 in Participants with Metastatic or Locally Advanced Unresectable Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma or Metastatic Pancreatic Adenocarcinoma (ASTELLAS). Continued	• 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. • 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: MRTX1719 in Patients With Advanced Solid Tumors With Homozygous MTAP Deletion (MIRATI 1719-001)

Study Design: The study is a Phase 1/2, open-label, multicenter, study of the safety, tolerability, PK, PD, and anti-tumor activity of MRTX1719 patients with advanced, unresectable or metastatic solid tumor malignancy with homozygous deletion of the MTAP gene.

NCT#: NCT05245500 **Study PI:** Dr. Ben George **Clinical Research Coordinator:** Nicholas Pucek **Phone:** 414-805-4639	***Key Inclusion:*** • Histologically confirmed diagnosis of a solid tumor malignancy with homozygous deletion of the MTAP gene detected in tumor tissue or ctDNA • Unresectable or metastatic disease • Patients must have received standard therapies appropriate for their tumor type and stage with disease progression on or after the most recent treatment ◦ Phase 1 dose escalation, RECIST 1.1 measurable or evaluable disease ◦ Phase 1b and Phase 2 cohorts, RECIST 1.1 measurable disease · • Presence of a tumor lesion amenable to mandatory biopsy for pharmacodynamic evaluation at baseline and on-study unless Sponsor-confirmed as medically unsafe or infeasible • ECOG: 0 or 1 ***Key Exclusion:*** · • Prior treatment with a PRMT5 or MAT2A inhibitor therapy. • Active brain metastases or carcinomatous meningitis. • History of significant hemoptysis or hemorrhage within 4 weeks of the first dose of study treatment. • Major surgery within 4 weeks of first dose of study treatment. • History of intestinal disease, inflammatory bowel disease, major gastric surgery, or other gastrointestinal conditions (eg, uncontrolled nausea, vomiting, malabsorption syndrome) likely to alter absorption of study treatment or result in inability to swallow oral medications • Cardiac abnormalities

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. Ben George

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
- 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

Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy for Patients (IIT-GEORGE-I-PREDICT) Continued	• 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

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:
Megan Graham
Phone: 414-805-8921

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.

Clinical Trial Name: HARPOON HPN328-4001: A Phase I/II Open-label, Multicenter, Dose Escalation and Dose Expansion Study of the Safety, Tolerability, and Pharmacokinetics of HPN328 Monotherapy and, HPN328 with Atezolizumab or Ifinatamab Deruxtecan (I-DXd) in Patients with Advanced Cancers Associated with Expression of Delta-like Canonical Notch Ligand 3 (DLL3)

Study Design: Characterize the impact of HPN328 on peripheral blood mononuclear cell (PBMC) and soluble serum cytokines, including but not limited to interferon gamma (IFNγ), interleukin (IL)-6, and tumor necrosis factor alpha (TNFα). Then assess DLL3 expression levels and associate with tumor response or treatment toxicity.

NCT#: NCT04471727

Study PI: Jonathan Thompson, MD

Clinical Research Coordinator:
Colleen Cotter
Phone: 414-805-8839

Key Inclusion:

- Histologically or cytologically confirmed high-grade malignancy associated with expression of DLL3. Pre-screening of tissue required and DLL3 expression demonstrated in a tumor sample in pre-screening.
- Disease that is relapsed/refractory to standard systemic therapy, Disease for which standard therapy does not exist, or Disease for which standard therapy is not considered appropriate by the Investigator.
- Inpatient admission required for study treatment.

Key Exclusion:

- Pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (e.g., biweekly or more frequently, or requiring indwelling catheter drain).
- Active or history of autoimmune disease or immune deficiency.
- History of arterial thrombosis (e.g., stroke or transient ischemic attack) within 6 months of the first dose of study drug.
- Patient received prior therapy with a DLL3 targeted agent.