METASTATIC

PHASE I/II STUDIES

Clinical Trial Name: 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).

Study Design: 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 Whose Tumors Have Claudin (CLDN) 18.2 Expression.

NCT #:

NCT05365581

Study PI: Dr. Mandana Kamgar

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. • 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: A Phase Ib/II Study of the Microenvironment Modifier L-DOS47 Plus Doxorubicin for the Treatment of Patients with Previously Treated Advanced Pancreatic Cancer (HELIX-LDOS006).	
Study Design: This is a open-label, single arm study that includes an initial three cohort dose escalation phase with 3, 6 and 9 µg/kg of L-DOS47 in combination with doxorubicin.	
NCT #: NCT04203641 **Study PI:** Dr. Ben George **Research Coordinator:** Nick Pucek **Phone:** 414-805-3158	***Key Inclusion****:* • ≥1 metastatic tumors measurable on CT scan per RECIST version 1.1 and screening FDG-PET scan with maximum standardized uptake value (SUV max) ≥ 5.5 for at least one lesion consistent with pancreatic cancer. • Karnofsky performance status ≥ 70%. • Acceptable liver function: Bilirubin ≤ 1.5 times upper limit of normal; Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and Alkaline phosphatase (ALP) ≤ 2.5 times upper limit of normal (ULN; if liver metastases are present, then ≤ 5 x ULN is allowed); Acceptable renal function as defined by creatinine ≤1.5x institutional upper limits of normal, or calculated creatinine clearance ≥ 60 mL/min/1.73 m2 for patients with creatinine levels above institutional normal; Acceptable hematologic status: Granulocyte ≥ 1500 cells/mm3; Platelet count ≥ 100,000 (plt/mm3); Hemoglobin ≥ 9g/dL • Urinalysis: No clinically significant abnormalities. • Acceptable coagulation status: Prothrombin time within 1.5x of normal limits; Partial thromboplastin time (PTT) within 1.5x of normal limits. • Normal ejection fraction on ECHO or MUGA. ***Key Exclusion****:* • New York Heart Association Class III or IV, cardiac disease, myocardial infarction within the past 6 months, unstable arrhythmia, or evidence of ischemia on ECG. • Abnormal ejection fraction on ECHO or MUGA. • Active, uncontrolled bacterial, viral, or fungal infections requiring systematic therapy. • Treatment with radiation therapy, surgery, chemotherapy, or investigational therapy within 3 weeks prior to study entry. • Serious nonmalignant disease (eg hydro nephrosis, liver failure, or other conditions) that could compromise protocol objectives in the opinion of the investigator and/or the sponsor. • Patients with marked screening prolongation of QT/QTc interval (e.g. repeated demonstration of a QTc interval > 480 milliseconds (CTCAE grade 1) using Fredericia's QT correction formula.

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

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: Ben George

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

Research Coordinator: Paola Gonzalez Quevedo **Phone:** 414-805-2674	▪ 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 • 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.