

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 $\geq$ 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	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
Study PI: Dr. Mandana Kamgar	
Clinical Research Coordinator: Nicholas Pucek Phone: 414-805-4639	

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 $\geq 30\%$ 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 $\geq 1.0 \times 10^9/L$
 - Platelet count $\geq 75 \times 10^9/L$ § Total bilirubin $\leq 2.0 \times$ institution's upper limit of normal (ULN)
 - Patients without underlying liver disease: alanine transaminase (ALT) and aspartate aminotransferase (AST) $\leq 3 \times$ institutional ULN
 - Serum creatinine $\leq 2.0 \times$ 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
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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

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) $\geq 1.5 \times 10^9/L$ without granulocyte colony-stimulating factor support
 - White Blood Cell Count (WBC) count $\geq 2.5 \times 10^9 /L$ (2500/uL)
 - Lymphocyte count $\geq 0.5 \times 10^9/L$ (500/uL)
 - Platelet count $\geq 100 \times 10^9/L$ (100,000/uL) without transfusion
 - Hgb ≥ 9.0 g/dL
- Aspartate aminotransferase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) $\leq 2.5X$ 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 $\leq 1.5X$ ULN, unless in patients with known Gilbert disease ($\leq 3X$ 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) $\leq 1.5X$ 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.

Study PI:
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Clinical Research Coordinator:
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- 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 $\leq 2X$ 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	
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