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. Aditya Shreenivas

Research Coordinator:
Olivia Gorman

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: Phase I/II Study of the Safety, Pharmacokinetics, and Preliminary Clinical Activity of BT5528 in Patients with Advanced Malignancies Associated with EphA2 Expression (BICYCLE-BT5528-100)	
Study Design: Phase I/II multi-center, open-label trial will evaluate BT5528 administered once-weekly as a single agent and in combination with nivolumab.	
NCT #: NCT04180371 **Study PI:** Dr. Johnathan Thompson **Research Coordinator:** Catherine Feffer **Phone:** 414-805-8838	***Key Inclusion:*** • ECOG= 0 or 1. • Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. • Acceptable renal, hepatic, hematologic and coagulation functions. • All patients must have tumor tissue (fresh or archived) available for analysis of EphA2 tumor expression and other biomarkers. In the absence of available tumor tissue, patients must be willing to undergo a biopsy to provide fresh tumor samples. • Life expectancy ≥12 weeks after the start of BT5528 treatment according to the Investigator's judgment. • Must be willing and able to comply with the protocol and study procedures. • Additional inclusion criteria for Phase I (dose escalation phase, with BT5528 alone or in combination with nivolumab): ▪ Metastatic recurrent histologically confirmed malignant solid tumors historically known for high EphA2 tumor expression. Confirmation of EphA2 expression prior to enrollment is not required for participants with ovarian cancer and specific other individual tumor types. ▪ Exhausted all appropriate treatment options per local guidelines • Additional inclusion criteria for Phase II (dose expansion phase, with BT5528 alone): ▪ Participants with metastatic recurrent disease histologically confirmed to be non-small cell lung cancer, ovarian cancer, triple-negative breast cancer (TNBC), gastric/upper gastrointestinal (GI) cancer, head and neck (H&N) cancer, urothelial cancer are eligible and must have failed or are ineligible for all appropriate treatment options per local guidelines and must have evidence of radiographic progression on the most recent line of therapy. ▪ Patients with urothelial cancer who have previously received treatment with enfortumab vedotin (EV) are eligible to the study. Patients who received EV and showed disease progression within 6 months of treatment start are planned for less than 50% of total patients enrolled in the cohort. ***Key Exclusion:*** • Experimental treatments within 4 weeks of first dose of BT5528. • Prior toxicities must have resolved to Grade 1 per CTCAE v 5.0 (except alopecia which can be Grade 2). • Current treatment with strong inhibitors or inducers of CYP3A4 or strong inhibitors of P-gp. • Major surgery (excluding placement of vascular access) within 4 weeks of first dose of BT5528 study treatment and must have recovered adequately prior to starting study therapy. • Receipt of live vaccine within 30 days of study treatment. • Untreated CNS metastases or leptomeningeal disease.

	• Uncontrolled hypertension (systolic BP ≥160 mmHg or diastolic BP ≥100 mmHg that is not responsive to intervention) at screening or prior to initiation of study drug. • History or current evidence of any condition, therapy or laboratory abnormality that might confound the results of the study, interfere with the patient's participation: ▪ Patients with history of a cerebral vascular event (stroke or transient ischemic attack), unstable angina, myocardial infarction, congestive heart failure or symptoms of New York Heart Association Class III-IV documented within 6 months prior to first dose of BT5528 or: (i) Mean resting corrected QT interval (QTcF) >470 msec (ii) Any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, hypokalemia, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years-of-age, or any concomitant medication known to prolong the QT interval (iii) Any clinically important abnormalities (as assessed by the Investigator) in rhythm, conduction, or morphology of resting electrocardiograms (ECGs), e.g., complete left bundle branch block, third degree heart block • Known human immunodeficiency virus (HIV) or acquired immune deficiency syndrome (AIDS). Note: Well controlled HIV will be allowed if the patient meets all the following criteria at inclusion: ▪ CD4+ T-cell (CD4+) counts ≥350 cells/uL; HIV viral load <400 copies/mL; without a history of opportunistic infection within the last 12 months. ▪ On established antiretroviral therapy (ART) for at least 4 weeks. Use of anti-retroviral therapy is permitted, but should be discussed with the Medical Monitor on a case-by-case basis. • Patients with a positive hepatitis B surface antigen and/or anti-hepatitis B core antibody. Patients with a negative polymerase chain reaction (PCR) assay are permitted with appropriate antiviral therapy. • Active hepatitis C infection with positive viral load if hepatitis C virus (HCV) antibody positive (if antibody is negative then viral load not applicable). Patients who have been treated for hepatitis C infection can be included if they have documented sustained virologic response of ≥12 weeks. • Thromboembolic events and/or bleeding disorders 3 months (e.g., deep vein thrombosis [DVT] or pulmonary embolism [PE]) prior to first dose. • Prior history of pneumonitis with presence of residual symptoms. • History of another malignancy within 3 years before the first dose of BT5528, or any evidence of residual disease from a previously diagnosed malignancy (excluding adequately treated with curative intent basal cell carcinoma, squamous cell of the skin, cervical intraepithelial neoplasia/cervical carcinoma in situ or melanoma in situ or ductal carcinoma in situ of the breast). • Systemic anti-infective treatment or fever within the last 14 days prior to first dose of BT5528 study treatment.

Clinical Trial Name: A Phase I Clinical Trial to Evaluate the Safety, Tolerability and Pharmacokinetics of TST001 in Patients with Locally Advanced or Metastatic Solid Tumors (MABSPACE-TST001-1001)	
Study Design: This is an open label Phase I/IIa, First in Human trial of TST001, a recombinant humanized anti-Claudin 18.2 (CLDN18.2) IgG1 monoclonal antibody as monotherapy or in combination with nivolumab or standard of care. It is being tested against advanced and/or metastatic solid tumors including gastric, gastroesophageal junction, pancreatic cancers.	
NCT #: NCT04396821 **Study PI:** Dr. Ben George	***Key Inclusion****:* • Histologically or cytologically confirmed, locally advanced or metastatic solid tumors. • Part A only: ▪ Patients must be a) progressed after standard therapies, b) intolerant of standard therapies, or c) with a tumor type without standard therapy. • Part B only:

Research Coordinator: **Phone:** Gabrielle Threatt **Phone:** 414-805-4767	▪ Cohort A: Patients with previously untreated, unresectable, locally advanced or metastatic GC/GEJ adenocarcinoma; prior adjuvant or neoadjuvant therapy are allowed only if disease progressed or recurred at least 6 months after completion of these treatments. Patients may have received one infusion of mFOLFOX6 plus nivolumab during the screening period. ▪ Cohort B: Patients with GC/GEJ adenocarcinoma who have radiologically progressed following one or two prior systemic therapies; adjuvant or neoadjuvant therapy could be regarded as one line of therapy only if disease progressed or recurred during these treatments or within 6 months or less after completion of these treatments. ▪ Cohort C: Patients with previously untreated, unresectable, locally advanced or metastatic histologically confirmed pancreatic adenocarcinoma; prior adjuvant or neoadjuvant therapy are allowed only if disease progressed or recurred at least 6 months after completion of these treatments. Patients may have received up to 2 infusions of Gemcitabine + albumin-bound paclitaxel (with one week between each infusion) during the screening period. • ECOG= 0-1. ***Key Exclusion**:* • Symptomatic central nervous system metastases. • Prior treatment with any CLDN18.2 target agents. • Allergy or sensitivity to TST001 or known allergies to comparable drugs. • Severe cardiovascular disease, including CVA, TIA, myocardial infarction, or unstable angina, NYHA class III or IV heart failure or uncontrolled arrhythmia within 6 months of study entry, severe QTc prolongation, concomitant risks for QTc prolongation. • Concurrent malignancy within 5 years prior to entry except adequately treated certain types of cancer. • Active and clinically significant infections, known uncontrolled infections with hepatitis B, hepatitis C, known human immunodeficiency virus with acquired immunodeficiency syndrome related illness.

Clinical Trial Name: A Study of Multiple Immunotherapy-Based Treatment Combinations in Participants with Metastatic Pancreatic Ductal Adenocarcinoma (HOFFMANN-WO39608-MORPHEUS)	
Study Design: A Phase Ib/II, Open-label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Immunotherapy-based Treatment Combinations in Patients with Metastatic Pancreatic Ductal Adenocarcinoma	
NCT #: NCT03193190 **Study PI:** Dr. Ben George **Research Coordinator:** Aliece Novitski **Phone:** 414-805-3158	***Key Inclusion**:* • ECOG= 0 or 1 • Histologically or cytologically confirmed metastatic pancreatic ductal adenocarcinoma • For patients in Cohort 1: no prior systemic treatment for PDAC • For patients in Cohort 2: disease progression during administration of either 5-FU- or gemcitabine-based first-line chemotherapy • Life expectancy greater than or equal to 3 months • Availability of a representative tumor specimen that is suitable for determination of programmed death-ligand 1 (PD-L1) and/or additional biomarker status via central testing • Measurable disease (at least one target lesion) according to RECIST v1.1 • Adequate hematologic and end-organ function test results • Tumor accessible for biopsy ***Key Exclusion**:* • Uncontrolled pleural effusion, pericardial effusion, or ascites requiring drainage procedure (i.e., more than one time per month) • Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases • History of leptomeningeal disease • Active or history of autoimmune disease or immune deficiency

	• History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan • Active hepatitis B or C virus infection or active tuberculosis • Severe infection within 4 weeks prior to initiation of study treatment • Prior allogeneic stem cell or solid organ transplantation • History of malignancy other than pancreatic carcinoma within 2 years prior to screening, with the exception of those with a negligible risk of metastasis or death

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:** Catherine Feffer **Phone:** 414-805-8838	***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: Tumor-Agnostic Precision Immuno-oncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial

Study Design: A study to evaluate the efficacy and safety of multiple therapies that are selected using somatic alterations and potential predictive biomarkers identified via NGS assays in patients with solid tumors.

NCT #: NCT04589845 **Study PI:** Dr. Ben George **Research Coordinator:** Catherine Feffer **Phone:** 414-805-8838	***Key Inclusion:*** • Histologically or cytologically confirmed diagnosis of advanced and unresectable or metastatic solid malignancy. • Measurable disease as defined by Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1), Response Assessment in Neuro-Oncology (RANO) criteria, or International Neuroblastoma Response Criteria (INRC). • Performance status as follows: Participants aged >= 18 years: ECOG=0-2; Participants aged 16 to < 18 years: Karnofsky score >= 50%; Participants aged < 16 years: Lansky score >= 50% • For participants aged >= 18 and <18 years: adequate hematologic and end-organ function • Disease progression on prior treatment, or previously untreated disease with no available acceptable treatment • Adequate recovery from most recent systemic or local treatment for cancer • Life expectancy >= 8 weeks • Ability to comply with the study protocol, in the investigator's judgment • For female participants of childbearing potential: Negative serum pregnancy test <= 14 days prior to initiating study treatment; agreement to remain abstinent or use single or combined contraception methods that result in a failure rate of < 1% per year for the period defined in the cohort-specific inclusion criteria; and agreement to refrain from donating eggs during the same period • For male participants: Willingness to remain abstinent or use acceptable methods of contraception as defined in the cohort-specific inclusion criteria • In addition to the general inclusion criteria above, participants must meet all the cohort-specific inclusion criteria for the respective cohort ***Key Exclusion:*** • Any anticancer treatment within 2 weeks or 5 half-lives prior to start of study treatment. • Whole brain radiotherapy within 14 days prior to start of study treatment. • Stereotactic radiosurgery within 7 days prior to start of study treatment. • History of or concurrent serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the participant's safe participation in and completion of the study or confounds the ability to interpret data from the study. • Incomplete recovery from any surgery prior to the start of study treatment that would interfere with the determination of safety or efficacy of study treatment. • Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or higher), myocardial infarction, or cerebrovascular accident within 3 months prior to enrollment, unstable arrhythmias, or unstable angina. • History of another active cancer within 5 years prior to screening that may interfere with the determination of safety or efficacy of study treatment with respect to the qualifying solid tumor malignancy.

Clinical Trial Name: Study of Nab-Paclitaxel and Gemcitabine With or Without SBP-101 in Pancreatic Cancer (PANBELLA-CL-SBP-101-04)
Study Design: The study is a randomized, double-blind, placebo-controlled, multicenter study of standard treatment with nab-paclitaxel and gemcitabine with or without SBP-101 in subjects previously untreated for metastatic pancreatic ductal adenocarcinoma (PDA), including subjects who have received prior neoadjuvant or adjuvant treatment.

NCT #: NCT05254171 **Study PI:**	***Key Inclusion:*** • Histologically or cytologically confirmed metastatic pancreatic ductal adenocarcinoma. Subjects with pancreatic acinar cell carcinoma may also be included. • Previously untreated for metastatic pancreatic ductal adenocarcinoma; metastatic disease must have been diagnosed within the past 3 months; and subject is expected to receive standard treatment with gemcitabine and nab-paclitaxel. Subjects who have had planned or prior surgery, such as a Whipple procedure, with or without neo-adjuvant/adjuvant chemotherapy may be included. • Life expectancy ≥ 3 months.

Dr. Mandana Kamgar	• Measurable disease on computed tomography (CT) or magnetic resonance imaging (MRI) scan by RECIST v1.1 criteria. • ECOG Performance Status= 0-1. • Adequate bone marrow, hepatic and renal function as outlined in protocol. • Corrected QT interval (QTc); QTc interval ≤ 470 msec at Baseline. ***Key Exclusion:*** • BRCA (BReast CAncer gene antigen) positive. • Subjects taking metformin. Diabetic subjects on treatment with metformin, or any other derivative thereof, must discontinue it while on study (other diabetic medications are allowed). • History of retinopathy or macular degeneration. • Presence of islet-cell or pancreatic neuroendocrine tumor or mixed adenocarcinoma-neuroendocrine carcinoma. • CNS malignancy or metastasis. Screening of asymptomatic subjects without history of CNS metastases is not required. • Serum albumin < 30 g/L (3.0 g/dL). • Occurrence of deep vein thrombosis (DVT) or portal vein occlusion, pulmonary embolism (PE), or other thromboembolic event during screening. • Presence of interstitial lung disease, pulmonary fibrosis, or pulmonary hypersensitivity reaction. • Myocardial infarction within the last 12 months, severe/unstable angina, symptomatic congestive heart failure New York Heart Association (NYHA) class III or IV. • Any history of hydroxychloroquine use (Plaquenil® and other brand names).
Research Coordinator: Barb Dion **Phone:** 414-805-4639	