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A Phase 1 study of PHST001, an anti-CD24 monoclonal antibody, in adult patients with advanced relapsed and/or refractory solid tumors

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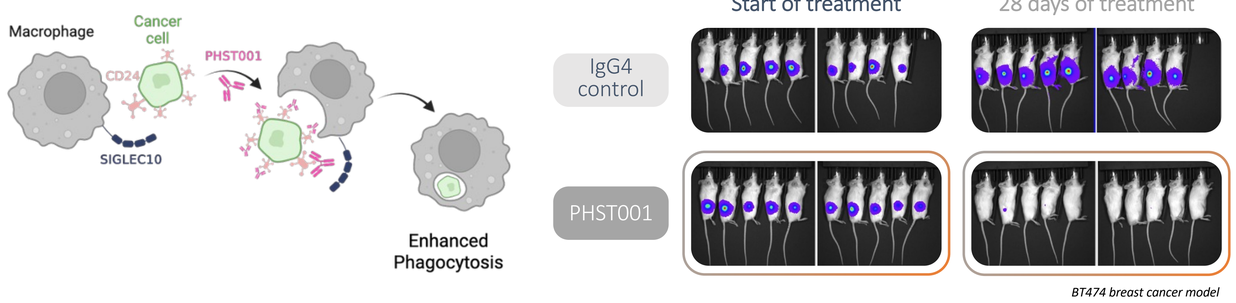
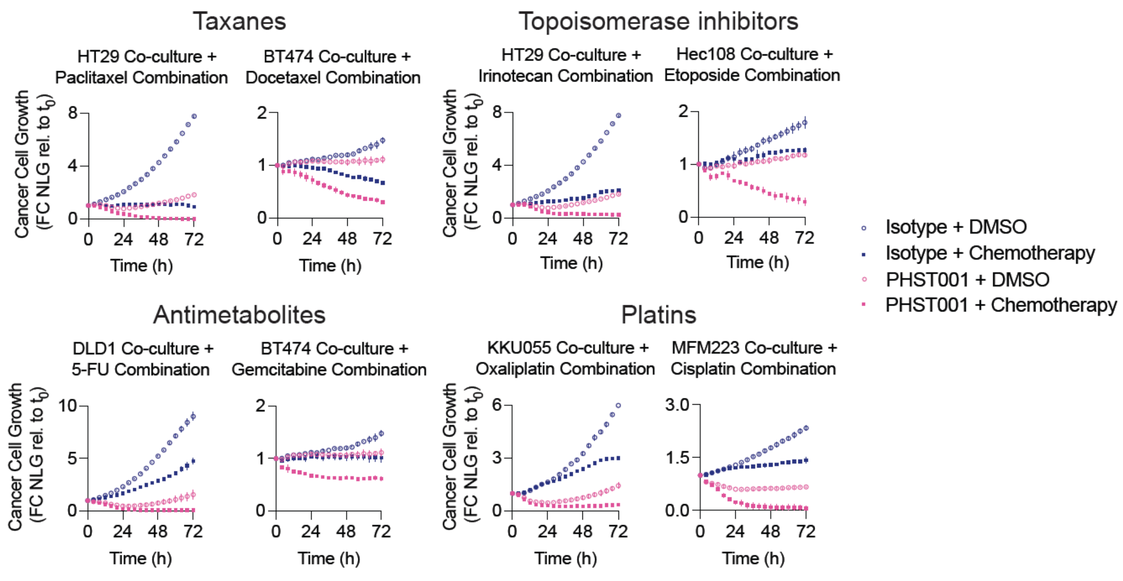
Background

- Tumor-associated macrophages can make up to 50% of the mass of solid tumors.[1] These macrophages have the potential to phagocytose tumor cells and induce T-cell immune responses,[2,3] yet are not targeted by currently available immunotherapies
- CD24 (Cluster of differentiation 24) is an immunomodulatory receptor overexpressed on the surface of many cancer cells, and mediates immune evasion by binding to Siglec-10 (Sialic-acid-binding Ig-like lectin-10) expressed on macrophages to prevent them from phagocytosing malignant cells[4,5]
- CD24 overexpression in various cancers—including ovarian, endometrial, breast, colorectal, lung, and cholangiocarcinoma—occurs through mechanisms including oncogenic amplification of the *CD24* locus, and is associated with poor survival outcomes[6-10]
- PHST001, a humanized IgG4 anti-CD24 monoclonal antibody, blocks the interaction of CD24 and Siglec-10 to induce phagocytosis of tumor cells, and demonstrates anti-tumor activity in preclinical models of ovarian, breast, endometrial, cholangiocarcinoma, and small cell lung cancer[11,12,13]



- PHST001-101 is a first-in-human clinical study of PHST001 in participants with advanced relapsed and/or refractory solid tumors as monotherapy (Phase 1a) or in combination with chemotherapy (Phase 1b) evaluating the safety, tolerability, PK, and anti-tumor activity of PHST001 (NCT06840886)

Selected chemotherapy agents combine with PHST001 to induce macrophage dependent cancer cell killing in vitro



Objectives and endpoints

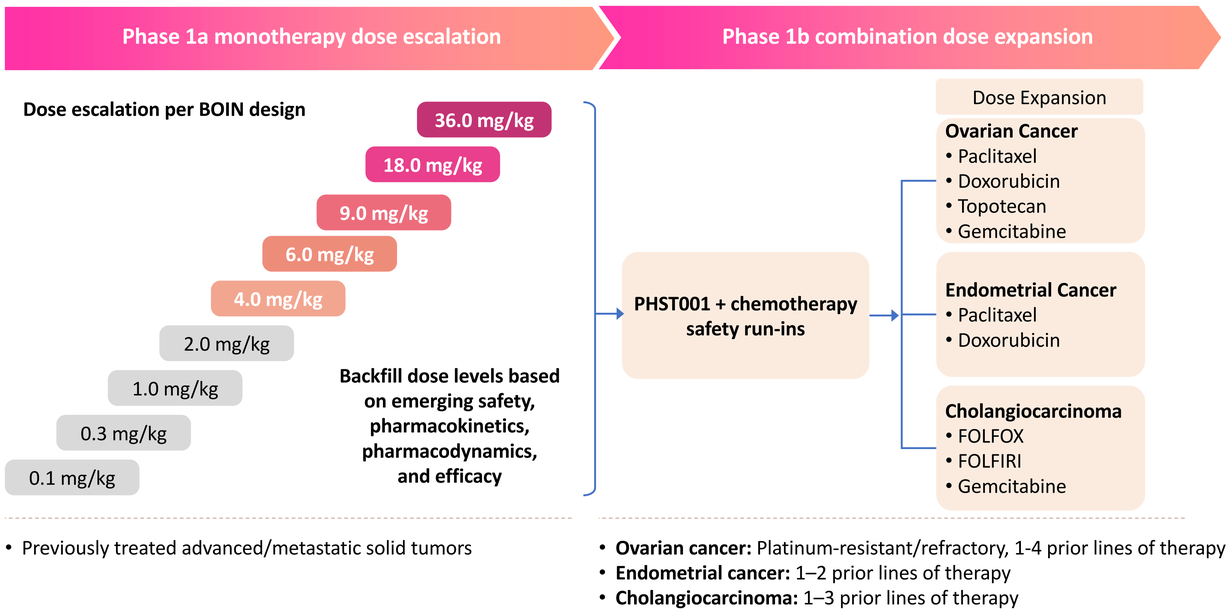
Primary Objectives	Primary Endpoints
• To assess the safety and tolerability of PHST001 as monotherapy (Phase 1a) or in combination with chemotherapy (Phase 1b) • To assess the preliminary antitumor activity of PHST001 in combination with chemotherapy (Phase 1b)	• Frequency of DLTs, SAEs, TEAEs, AESIs, and AEs leading to dose interruption, treatment discontinuation, or death • PHST001 in combination with chemotherapy: Investigator-assessed ORR, DOR, BOR, PFS, and OS per RECIST v1.1
Secondary Objectives	**Secondary Endpoints**
• To assess the preliminary antitumor activity of PHST001 as monotherapy (Phase 1a) • To characterize the serum PK of PHST001	• PHST001 monotherapy: Investigator-assessed ORR, DOR, BOR, PFS, and OS per RECIST v1.1 • Serum PK parameters
Exploratory Objectives	**Exploratory Endpoints**
• To assess biomarkers of pharmacodynamic response to PHST001 • To assess the immunogenicity of PHST001 (Phase 1a and Phase 1b) • To assess the preliminary antitumor activity in participants treated beyond progression • To assess the tolerability of PHST001 from the participant perspective	• Target occupancy, cytokine profiling, quantification of ctDNA, and analysis of immune cells in peripheral blood • Target expression, amplification status of CD24 genomic locus, immune cell frequency, and immune cell states in the TME when tumor biopsy is available • Prevalence at baseline and frequency of ADA formation against PHST001

Trial status

- **The study opened in March 2025, with an estimated enrollment goal of approximately 155 patients**
  - **As of May 2026, 17 sites across the United States are active**
  - **The first patient was treated in April 2025**
- **Patients are being enrolled into:**
  - **Phase 1a PHST001 monotherapy dose-escalation at the 18 mg/kg dose level**
  - **Phase 1b PHST001+chemotherapy safety run-in**
- **The estimated study duration is approximately 4 years, with an estimated treatment duration of up to 2 years for each participant**

PHST001-101 is a first-in-human phase 1a/1b, open-label, dose-escalation and -expansion trial

PHST001 is administered via intravenous infusion every 3 weeks:
As monotherapy in Phase 1a and in combination with chemotherapy in Phase 1b.



- Previously treated advanced/metastatic solid tumors

- **Ovarian cancer:** Platinum-resistant/refractory, 1-4 prior lines of therapy
- **Endometrial cancer:** 1–2 prior lines of therapy
- **Cholangiocarcinoma:** 1–3 prior lines of therapy

Select inclusion and exclusion criteria

Inclusion criteria

- ≥18 years old
- ECOG performance status of 0 or 1
- Phase 1a: Histologically or cytologically confirmed advanced solid tumor that has relapsed from/been refractory to all locally available standard therapies
- Phase 1b: advanced/metastatic solid tumor including:
  - Epithelial ovarian, primary peritoneal, or fallopian tube carcinoma who have progressed and are platinum-resistant with at least 1 but no more than 4 prior lines of systemic therapy
  - Endometrial adenocarcinoma (regardless of mismatch repair status) who have progressed on at least 1, but no more than 3 prior lines of therapy
  - Cholangiocarcinoma who have progressed on at least 1, but no more than three prior lines of therapy
- Measurable disease per RECIST v1.1 as assessed by the local site investigator/radiology
- Adequate organ function
- Female patients must not be pregnant or breastfeeding, not of childbearing potential as per contraception guidance and/or of childbearing potential, and agree to comply with contraception requirements
- Male patients with a female partner(s) of childbearing potential must agree to comply with contraception requirements

Exclusion criteria

Medical conditions

- Diagnosis of immunodeficiency, active autoimmune disease that has required systemic treatment in the past 2 years, previous severe hypersensitivity reaction (Grade ≥3) to treatment with another monoclonal antibody, or history of hypersensitivity to any components or excipients of the study treatments
- History of a previous additional malignancy, unless potentially curative treatment has been completed, with no evidence of malignancy
- Active known CNS metastases and/or carcinomatous meningitis
- Active infection requiring systemic therapy
- Prior autologous/allogeneic hematopoietic stem cell, or solid organ transplant
- Known infection with HIV-1 or HIV-2, unless well controlled, current or known active liver disease from any infectious cause, including HBV and HCV
- Clinically significant heart disease that affects normal activities

Abbreviations: ADA, anti-drug antibody; AE, adverse event; AESI, adverse event of special interest; BOIN, Bayesian Optimal Interval; BOR, best overall response; BT474, human breast cancer cell line BT474; CD24, Cluster of differentiation 24; ctDNA, circulating tumor DNA; DLD1, human colorectal adenocarcinoma cell line DLD1; DLT, dose-limiting toxicity; DMSO, dimethyl sulfoxide; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; FC NLG, fold-change nuclear-localized green; FOLFIRI, combination regimen of folinic acid, fluorouracil and irinotecan; FOLFOX, combination regimen of folinic acid, fluorouracil and oxaliplatin; h, hour(s); HBV, hepatitis B virus; HCV, hepatitis C virus; Hec108, human endometrial carcinoma cell line Hec108; HIV, human immunodeficiency virus; HT29, human colorectal adenocarcinoma cell line HT29; IgG4, immunoglobulin G4; KKU055, human cholangiocarcinoma cell line KKU055; MFM223, human breast carcinoma cell line MFM223; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumors; rel., relative; SAE, serious adverse event; Siglec-10, sialic-acid-binding Ig-like lectin-10; t0, time zero; TEAE, treatment-emergent adverse event; TME, tumor microenvironment.

References: 1. Larionova I, *et al*. Tumor-associated macrophages in human breast, colorectal, lung, ovarian and prostate cancers. *Front Oncol*. 2020;10:566511; 2. Zhou X, *et al*. Macrophage-mediated tumor cell phagocytosis: opportunity for nanomedicine intervention. *Adv Funct Mater*. 2021;31(5):2006220; 3. Muntjewerff EM, *et al*. Antigen Cross-Presentation by Macrophages. *Front Immunol*. 2020;11:1276; 4. Barkal AA, *et al*. CD24 signalling through macrophage Siglec-10 is a target for cancer immunotherapy. *Nature*. 2019;572(7769):392-396; 5. Zhao K, *et al*. From mechanism to therapy: the journey of CD24 in cancer. *Front Immunol*. 2024;15:1401528; 6. Deng J, *et al*. CD24 expression as a marker for predicting clinical outcome in human gliomas. *J Biomed Biotechnol*. 2012;2012:517172; 7. Zhang P, *et al*. Amplification of the CD24 gene is an independent predictor for poor prognosis of breast cancer. *Front Genet*. 2019;10:560; 8. Gu Y, *et al*. The biological roles of CD24 in ovarian cancer: old story, but new tales. *Front Immunol*. 2023;14:1183285; 9. Liu H, *et al*. Metabolic genes interaction perturbation network identified and validated CD24 as a novel prognostic gene in hepatocellular carcinoma. *Discov Oncol*. 2025;16(1):1643; 10. Agarwal S, *et al*. CD24 expression is an independent prognostic marker in cholangiocarcinoma. *J Gastrointest Surg*. 2007;11(4):445-451; 11. Kahn SA, *et al*. PHST001, a humanized anti-CD24 antibody, induces phagocytosis of human tumor cells in vitro and tumor clearance in vivo (abstract no. 513). *J Immunother Cancer*. 2024;12(Suppl 2):A578-A581. 12. Kahn SA, *et al*. PHST001, a humanized anti-CD24 antibody, induces phagocytosis of ovarian tumor cells in vitro and inhibits their growth in vivo (abstract no. B052). *Cancer Res*. 2025;85(18 Suppl). 13. Data on file.

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