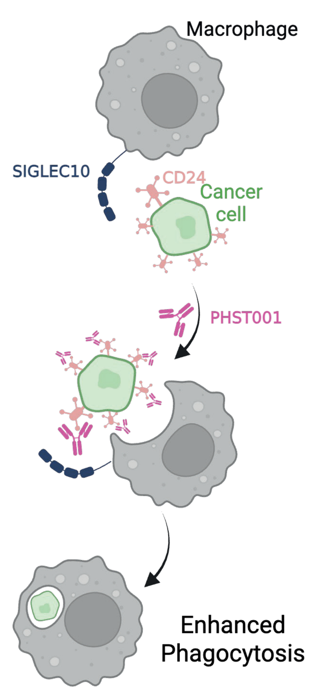
Phase 1 study of PHST001, a humanized anti-CD24 monoclonal antibody, in adult patients with advanced relapsed and/or refractory solid tumors

Kyri Papadopoulos[1], Gini F Fleming[2], Anthony El-Khoueiry[3], Oliver Dorigo[4], Michael J Dennis[5], Niharika B Mettu[6], Michael Cecchini[7], Ulka N Vaishampayan[8], Elizabeth J Davis[9], Jennifer Yinuo Cao[10], Suzana Kahn[10], Susan Luebbe[10], Raphaël Rousseau[10] and Stéphane Champiat[11]

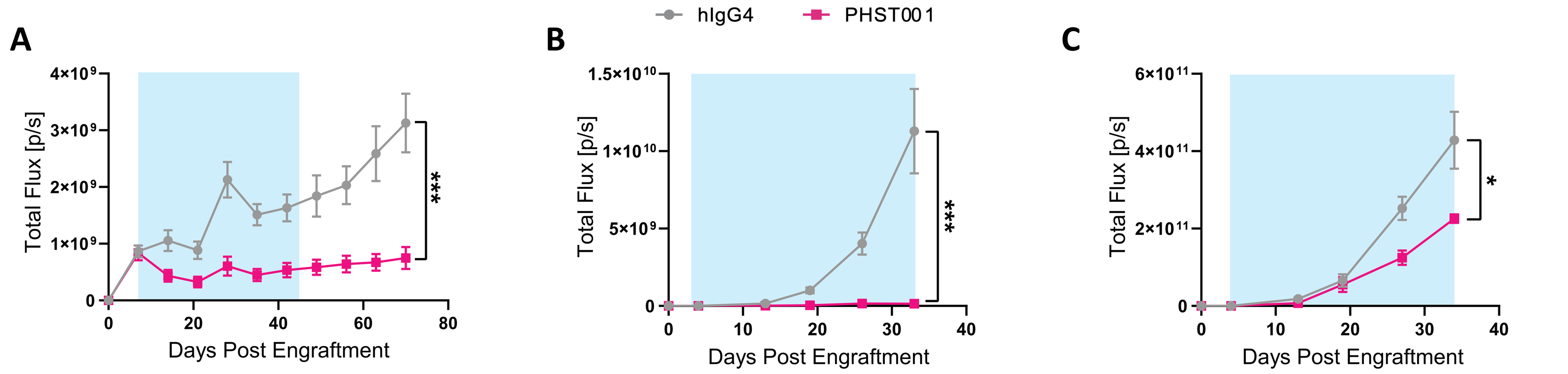
1. South Texas Accelerated Research Therapeutics (START), San Antonio, TX; 2. University of Chicago Medicine, Chicago, IL; 3. University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA; 4. Stanford Women's Cancer Center and Stanford Cancer Institute, Stanford, CA; 5. Dana–Farber Cancer Institute, Boston, MA; 6. Duke Cancer Center, Durham, NC; 7. Yale School of Medicine, New Haven, CT; 8. University of Michigan, Ann Arbor, MI; 9. Vanderbilt University Medical Center, Nashville, TN; 10. Pheast Therapeutics, Redwood City, CA; 11. Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Background

- CD24 (cluster of differentiation 24) is an immunomodulatory receptor overexpressed on the cell surface of many cancer cells that plays an important role in immune evasion[1,2]
  - Tumor-expressed CD24 functions as a "don't eat me" signal by binding to Siglec10 (sialic-acid-binding Ig-like lectin-10) on macrophages, preventing phagocytosis of malignant cells
- CD24 overexpression may be associated with poor survival outcomes in patients with certain cancers, including ovarian, breast, non-small cell lung, prostate, bladder and hepatocellular cancers, cholangiocarcinoma and glioma[3-7]
- PHST001 is a humanized IgG4 monoclonal antibody that binds to CD24 to disrupt the interaction between CD24 and Siglec-10, and induces phagocytosis and tumor clearance by macrophages[1]
  - PHST001 received FDA fast track designation for the treatment of advanced ovarian cancers in June 2025[8]
- A first-in-human phase 1a/1b, open-label, dose escalation, and expansion trial to evaluate safety, tolerability, PK, and antitumor activity of PHST001 in adult participants with advanced relapsed and/or refractory solid tumors is ongoing (**NCT06840886**)



PHST001 has robust monotherapy activity against cancer models in vivo



A. Ovarian cancer xenotransplantation model established by subcutaneously engrafting OVCAR-3 cells. Total tumor flux (mean ± SEM) of OVCAR-3 tumor-bearing mice treated with PHST001 20 mg/kg or isotype control over time (Student's *t* test, ***p<0.001).

B. Endometrial cancer xenotransplantation model was established by engrafting SNGM cells intraperitoneally. Total tumor flux (mean ± SEM) of SNGM tumor-bearing mice treated with PHST001 20 mg/kg or isotype control over time (Student's *t* test, ***p<0.001).

C. Cholangiocarcinoma xenotransplantation model was established by engrafting KKU-213 cells subcutaneously. Total tumor flux (mean ± SEM) of KKU-213 tumor-bearing mice treated with PHST001 20 mg/kg or isotype control over time (Student's *t* test, *p<0.05).

The blue area denotes the period when mice were subjected to treatment (3 times per week for a total of 18 doses).

Trial objectives

- Evaluate the safety, tolerability, recommended phase 2 dose, and antitumor activity of PHST001 as monotherapy or in combination with standard chemotherapeutic agents
- Characterize serum PK of PHST001 and assess its relationship with biomarkers of PD response
- Assess the immunogenicity of PHST001

Trial status

- The study opened in March 2025, with an estimated enrollment goal of approximately 155 patients
  - As of October 2025, 10 sites across the United States are active
  - First patient was treated in April 2025
- The study duration is estimated to be approximately 4 years, and the estimated treatment duration will be up to 2 years for each study participant
- A protocol amendment detailing the Phase 1b combination of PHST001 with chemotherapy is under review

Study design

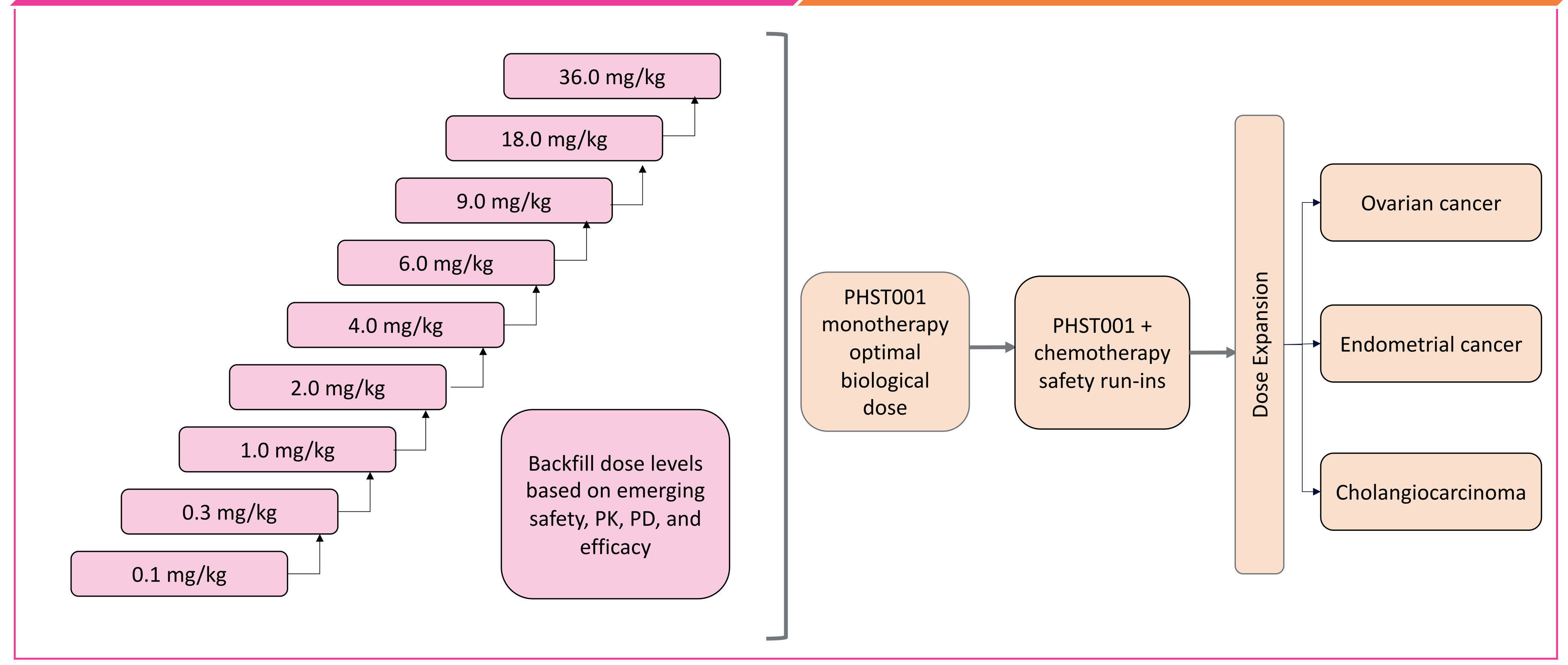
- Participants 18 years or above with advanced relapsed and/or refractory solid tumors will be enrolled to the dose escalation and expansion cohorts per the BOIN method
- The totality of safety, including that contributed by the backfill cohorts, will be continuously monitored by Bayesian posterior probability

Phase 1a

- Participants will receive escalating doses of PHST001 given Q3W as an IV infusion and may be eligible for intra-participant dose escalation
- Those in backfill cohorts will not be included in the DLT-evaluable population but may inform suitable a dose range for the phase 1b portion of the trial

Phase 1b

- PHST001 will be combined with chemotherapeutic agents used as standard of care
- The dose of PHST001 and/or the dose and/or schedule of the chemotherapeutic agent(s) may be modified by the safety review committee



Select endpoints

Primary	Secondary	Exploratory
• Frequency of DLTs, SAEs, TEAEs, TRAEs, AESIs, and AEs leading to dose interruption, treatment discontinuation, or death • PHST001 in combination with chemotherapy: Investigator-assessed ORR, DOR, BOR, PFS per RECIST v1.1 or RANO, and OS	• PHST001 monotherapy: Investigator-assessed ORR, DOR BOR, PFS, per RECIST v1.1 or RANO and OS • Serum PK parameters including, but not limited to, C_{max}, t_{max}, C_{trough}, AUC, V_{ss}, CL, and $t_{½}$	• 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

Key inclusion and exclusion criteria

Inclusion criteria

- Aged ≥18 years old
- ECOG performance status of 0 or 1
- Histologically or cytologically confirmed advanced solid tumor that has relapsed from/been refractory to all locally available standard therapies[†*]
- Measurable disease per RECIST v1.1 or RANO 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

- 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 for 5 years
- 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

*Phase 1b will include patients with previously treated solid tumors, according to tumor type-specific criteria; enrolment of tumor types and eligibility criteria will be determined based on the totality of data from Phase 1a and enacted based on the in-progress protocol amendment.

Abbreviations: ADA, antidrug antibody; AE, adverse event; AESI, adverse event of special interest; AUC, area under the concentration–time curve; BOIN, Bayesian Optimal Interval Design; BOR, best overall response; CD24, Cluster of differentiation 24; C_{max}, maximum observed concentration; CL, clearance; CNS, central nervous system; ctDNA, circulating tumor DNA; C_{trough}, concentration at the end of a dosing interval (i.e., just before next drug administration); DLT, dose-limiting toxicity; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; FDA, Food and Drug Administration; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IV, intravenous; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse event; SEM, standard error of the mean; Siglec-10, sialic-acid-binding Ig-like lectin-10; $t_{½}$, terminal elimination half-life; t_{max}, time to maximum concentration; TEAE, treatment-emergent adverse event; TME, tumor microenvironment; TRAE, treatment-related adverse event; V_{ss}, volume of distribution at steady state.

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Contact: Raphaël Rousseau, MD, PhD. raphael.rousseau@pheast.com

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