A phase 1, open label, multiple dose, dose escalation, and expansion study to investigate the safety, tolerability, pharmacokinetics, and antitumor activity of the PTK7-targeted antibody-drug conjugate DAY301 in patients with locally advanced or metastatic solid tumors

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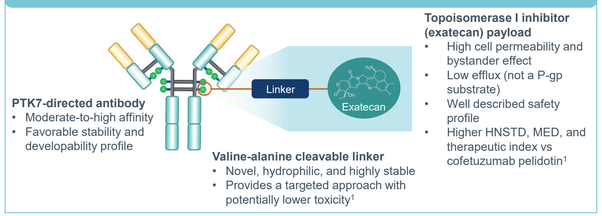
Background

- PTK7 is in the pseudokinase family of receptor tyrosine kinases and is an emerging therapeutic target for various solid malignancies due to overexpression on the tumor cell surface[1]
- DAY301 is a novel ADC composed of a humanized PTK7 monoclonal antibody, conjugated through a cleavable linker to an exatecan payload (**Figure 1**)[1]
  - DAY301 was designed to maximize the therapeutic index and overcome limitations of prior PTK7 programs, including toxicity[1]
  - The molecule has a DAR of 8,[1] which has been shown to be effective for other ADCs targeting solid tumors[2]
- DAY301 demonstrated potent antitumor activity at tolerable doses in a wide range of tumor PDX models (**Figure 2**)[1]
  - Cytotoxic activity was achieved through DNA damage and apoptosis induction, as well as a strong bystander effect[1]
- In a GLP 7-week repeat-dose toxicity study in cynomolgus monkeys, DAY301 was well tolerated with no treatment-related electrocardiographic, pulmonary, or ophthalmologic changes observed at all dose levels
- A first-in-human ph1a/1b, open-label, dose escalation, and expansion trial to evaluate the safety, tolerability, PK, and antitumor activity of DAY301 is ongoing (NCT06752681)[3]

Overview of PTK7

- Highly expressed at the cell surface in a number of adult and pediatric solid tumors, including ovarian, endometrial, HNSCC, and lung cancer[4,5]
- Transmembrane receptor with an inactive intracellular tyrosine kinase domain[6]
- Interacts with several signaling pathways, notably Wnt and VEGF[4,6]
- Is associated with metastasis, poor prognosis, and resistance to treatment[4]

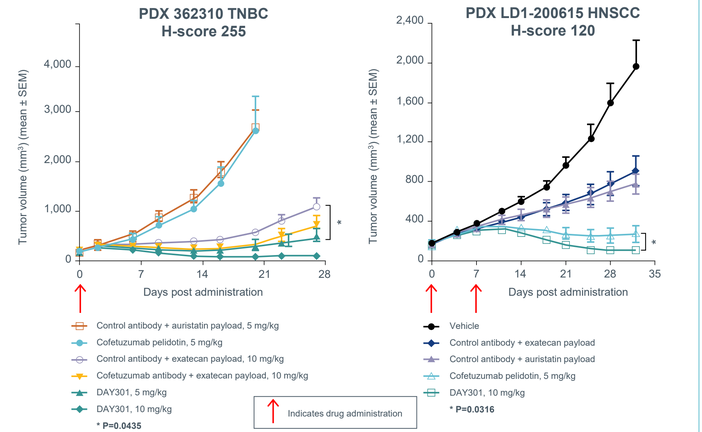
Figure 1. Overview of DAY301



Trial objectives

- Characterize the safety and tolerability of DAY301, and establish the maximum tolerated dose and recommended dose for expansion cohorts (ph1a)
- Evaluate the safety and preliminary efficacy of DAY301, as assessed by ORR (ph1b)

Figure 2. Improved tumor growth inhibition demonstrated for DAY301 versus benchmarks in multiple preclinical models of variable PTK7 expression[1]



Adapted from Kong C, *et al. Mol Cancer Ther.* 2023;22:1128–1143.

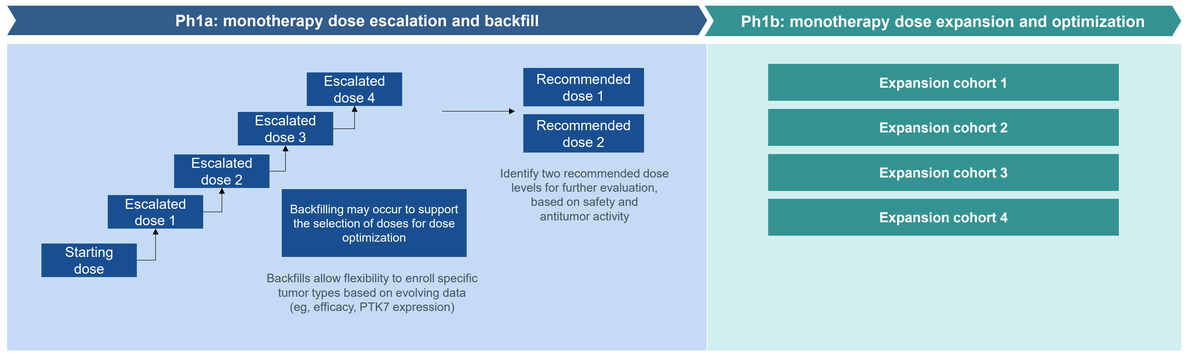
Methods: Ph1a

- Enrollment into the dose escalation cohorts is following a Bayesian Optimal Interval Design, except for the first dose cohort (**Figure 3**)
- DAY301 is being administered by intravenous injection once every 3 weeks
- Patients may be enrolled in backfill cohorts to further characterize safety, PK, and preliminary efficacy at dose levels that have been determined to be safe based on evaluation of DLTs during the first 21 days of treatment

Methods: Ph1b

- Enrollment into the tumor-specific dose expansion cohorts (**Figure 3**) will follow an optimal Simon's 2-stage design
  - PTK7 expression threshold for enrollment will be based on retrospective analysis from ph1a
- Patients will be treated with the recommended doses for expansion determined in ph1a
  - Lower doses may be explored based on emerging safety and efficacy data

Figure 3. DAY301-001 ph1a/1b trial design



Inclusion criteria

- Patients ≥18 years of age with advanced or metastatic solid tumors
- Available tumor tissue sample
- Measurable disease per RECIST v1.1
- ECOG PS of 0 or 1
- Adequate organ function
- Ph1a to include patients with tumors known to express PTK7:
  - OC
  - ESCC
  - TNBC
  - NSCLC
  - SCLC
  - HNSCC
  - Gastric/GEJ adenocarcinoma
  - CSCC
  - EC
- Ph1b: tumor types to be defined based on ph1a data and ongoing translational studies

Exclusion criteria

- Prior use of PTK7-targeting treatment
- Active or progressing brain metastases or evidence of leptomeningeal disease
- Persistent toxicity from prior treatments
- Chemotherapy within previous 4 weeks (or within 5 half-lives)
- Radiotherapy within previous 4 weeks
- Any of the following:
  - History of liver or bone marrow transplant
  - Significant cardiac disease
  - History of thromboembolic or cerebrovascular events
  - Corneal defects or transplant

Trial endpoints

Primary

Ph1a: Incidence of DLTs

Ph1a/1b: Incidence and severity of AEs and SAEs; frequency and duration of dose interruptions and reductions

Ph1b: ORR (investigator assessed per RECIST v1.1)

Secondary

Ph1a: Preliminary efficacy: ORR, CBR, DOR, TTR, and PFS (all investigator assessed per RECIST v1.1)

Ph1b: CBR, DOR, TTR, and PFS (all investigator assessed per RECIST v1.1)

Ph1a/1b: OS, anti-drug antibodies, PK parameters

Exploratory

Ph1a: DAR over time

Ph1a/1b: Predictive biomarkers, PTK7 expression and correlation with clinical response

Trial status

- Recruitment started in November 2024,[3] with a goal of ~84 and 116 patients maximum in ph1a and 1b, respectively
  - The first patient was enrolled in December 2024
  - Dose escalation is ongoing
- Based on the totality of data from ph1b, a RP2D for future clinical studies will be determined

References

1. Kong C, *et al. Mol Cancer Ther.* 2023;22(10):1128–1143.
2. Martín M, *et al. Crit Rev Oncol Hematol.* 2024;198:104355.
3. Clinicaltrials.gov (NCT06752681). https://clinicaltrials.gov/study/NCT06752681. Accessed March 14, 2025.
4. Dessaux C, *et al. Oncogene.* 2024;43:1973–1984.
5. Shin W-K, *et al. Sci Rep.* 2018;8:8519.
6. Mossie K, *et al. Oncogene.* 1995;11(10):2179–2184.

Abbreviations

ADC, antibody-drug conjugate; AEs, adverse events; CBR, clinical benefit rate; CSCC, cervical squamous cell carcinoma; DAR, drug-to-antibody ratio; DLT, dose-limiting toxicity; DNA, deoxyribonucleic acid; DOR, duration of response; EC, endometrial carcinoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ESCC, esophageal squamous cell carcinoma; GEJ, gastroesophageal junction; GLP, Good Laboratory Practice; HNSCC, head and neck squamous cell carcinoma; HNSTD, highest non-severely toxic dose; MED, minimum effective dose; NSCLC, non-small cell lung cancer; OC, ovarian cancer; ORR, overall response rate; OS, overall survival; P-gp, p-glycoprotein; PDX, patient-derived xenograft; PFS, progression-free survival; ph, phase; PK, pharmacokinetic; PTK7, protein tyrosine kinase 7; RECIST, response evaluation criteria in solid tumors; RP2D, recommended phase 2 dose; SAEs, serious adverse events; SCLC, small cell lung cancer; SEM, standard error of the mean; TNBC, triple negative breast cancer; TTR, time to response; VEGFR, vascular endothelial growth factor receptor, wnt, wingless-type MMTV integration site family.

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For more information on this trial, please visit clinicaltrials.gov/study/NCT06752681 or contact clinicaltrials@dayonebio.com