

Background

- CR-001 is a tetravalent bispecific antibody targeting programmed cell death-1 (PD-1) and vascular endothelial growth factor (VEGF) (Figure 1), designed to enhance antitumor activity through combined immune modulation and antiangiogenic effects.
- The proposed mechanism of action of CR-001 involves dual binding and blockade of both PD-1/programmed death ligand-1 (PD-L1) and VEGF/vascular endothelial growth factor receptor 2 (VEGFR2) signaling.
- The blockade of VEGF signaling is aimed at inhibiting tumor angiogenesis and reversing immunosuppressive effects in the tumor microenvironment, while PD-1 binding is aimed at preventing T-cell suppression, thereby promoting the immune recognition and elimination of tumor cells.
- The established benefit/risk profiles and regulatory precedents for PD-1-, VEGF-, and dual-pathway-directed antibodies support evaluation of CR-001 in solid tumors.
- In this poster, we describe the design of ASCEND, a global, first-in-human, open-label, phase 1/2 study evaluating CR-001 monotherapy in patients with locally advanced or metastatic solid tumors.

Figure 1. CR-001 is a highly potent PD-1 x VEGF bsAb

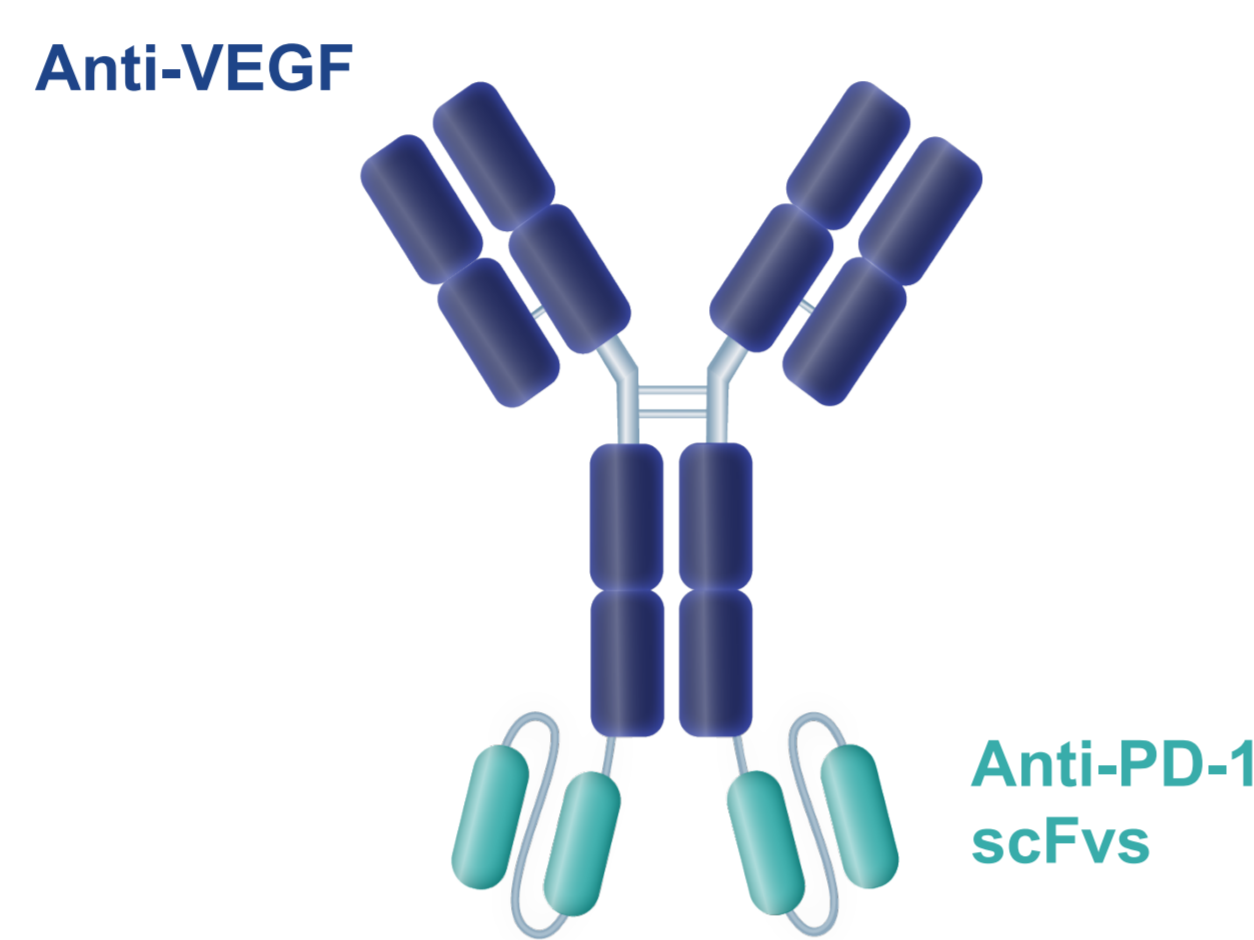
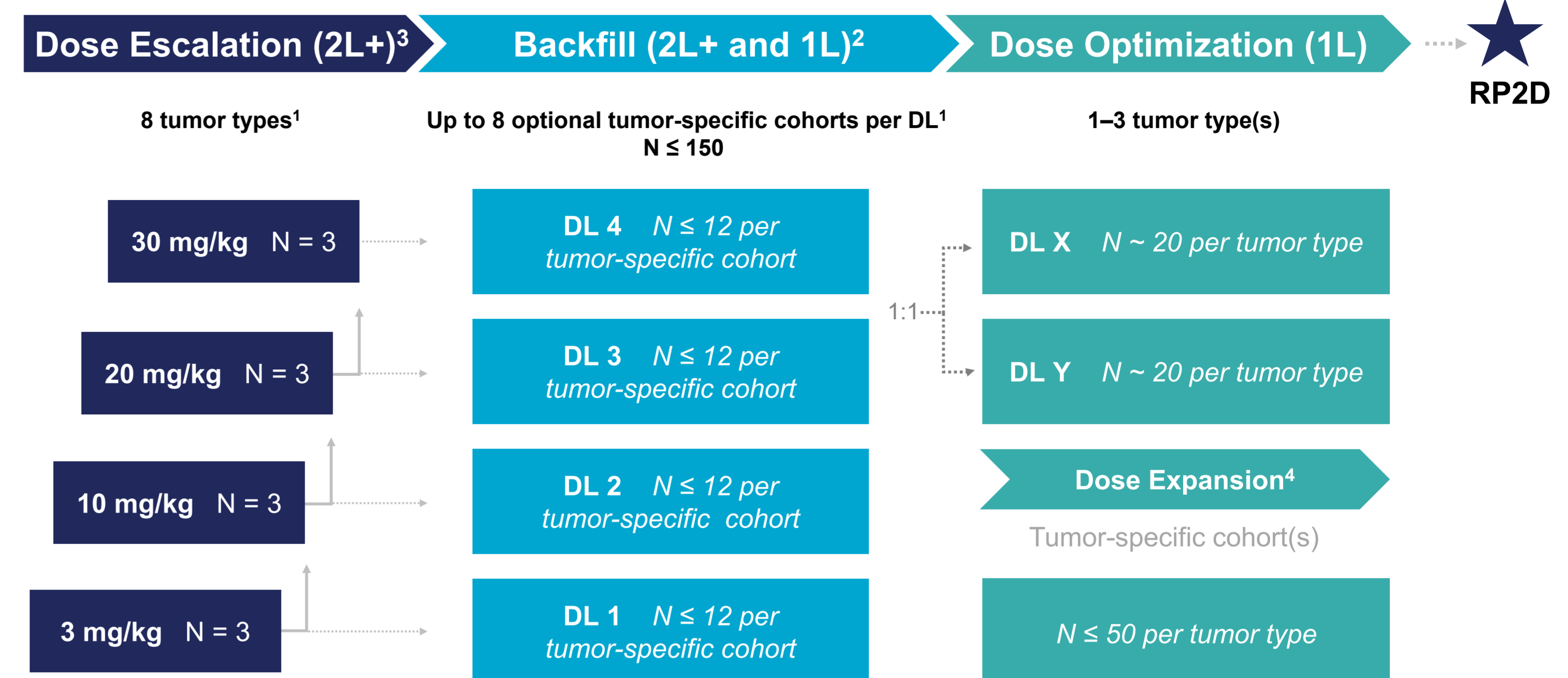


Figure 2. ASCEND study design



Abbreviations: DL, dose level; RP2D, recommended Phase 2 dose

Note: Dashed lines indicate backfill and expansion cohort optionality

- 8 tumor types: hepatocellular carcinoma, biliary tract cancer, gastric cancer, colorectal cancer, endometrial carcinoma, cervical cancer, ovarian cancer, and non-small cell lung cancer
- Dose regimens for backfill cohorts will be determined by emerging data and doses deemed adequately tolerated per the safety review committee. Each dose level may have up to 8 different tumor-specific cohorts that can enroll up to 12 participants each for a maximum of approximately 150 participants in backfill
- Dose escalation is conducted according to 3+3 design
- Selected dose-expansion tumor types may include tumor types from backfill or other solid tumor indications not previously evaluated

Methods

- ASCEND (NCT07335497) is a global, first-in-human, open-label, phase 1/2 study evaluating CR-001 monotherapy in adult participants with locally advanced or metastatic solid tumors.
- The purpose of this study is to determine the safety and tolerability of CR-001 and identify the maximum tolerated dose, and/or recommended phase 2 dose (RP2D).
- The study will initially involve three parts: dose escalation, backfill, and dose optimization (Figure 2).
- Key inclusion/exclusion criteria are detailed opposite.
- The RP2D will be determined based on review of pharmacokinetics/pharmacodynamics, safety, tolerability, and preliminary signs of antitumor activity.

Study objectives	Endpoints
Primary	
<ul style="list-style-type: none"> Characterize the safety and tolerability of increasing dose levels of CR-001 in successive cohorts of participants with locally advanced or metastatic solid tumors 	<ul style="list-style-type: none"> Incidence and nature of DLTs during Cycle 1 (28 days) of CR-001 administration, and MTD characterization, if applicable Incidence, nature, and severity of TEAEs and treatment-emergent SAEs, graded according to NCI CTCAE Severity and nature of TEAEs leading to dose modifications and treatment discontinuation
Secondary	
<ul style="list-style-type: none"> Identify the RP2D(s) of CR-001 based on the totality of safety, tolerability, PK, PD, and clinical activity data Characterize the PK profile of CR-001 Characterize the immunogenicity of CR-001 Characterize the preliminary antitumor activity of CR-001 	<ul style="list-style-type: none"> The RP2D will be determined based on a review of available safety, tolerability, PK, PD, and clinical activity data Serum PK parameters: AUC_{0-inf}, AUC_{last}, C_{max}, T_{max}, V_d, CL, and $t_{1/2}$ after a single dose and steady state PK parameters as appropriate Incidence of participants with detectable ADAs ORR, DOR, DCR, TTR, PFS, OS, and best percent change in target lesions

Abbreviations

ADAs, antidrug antibodies; AE, adverse event; AUC_{0-inf} , area under the curve from time 0 extrapolated to infinity; AUC_{last} , area under the concentration-time curve from time 0 to the time of the last quantifiable concentration; CL, clearance; C_{max} , maximum concentration; DLT, dose-limiting toxicity; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MTD, maximum tolerated dose; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PD-1, programmed cell death-1; PD-L1, programmed death ligand-1; PK, pharmacokinetics; PFS, progression-free survival; Q2W, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose; SAE, serious adverse event; $t_{1/2}$, elimination half-life; TEAE, treatment-emergent adverse event; T_{max} , time to maximum concentration; TTR, time to response; V_d , volume of distribution; VEGF, vascular endothelial growth factor; VEGFR2, vascular endothelial growth factor receptor 2.

Eligibility criteria

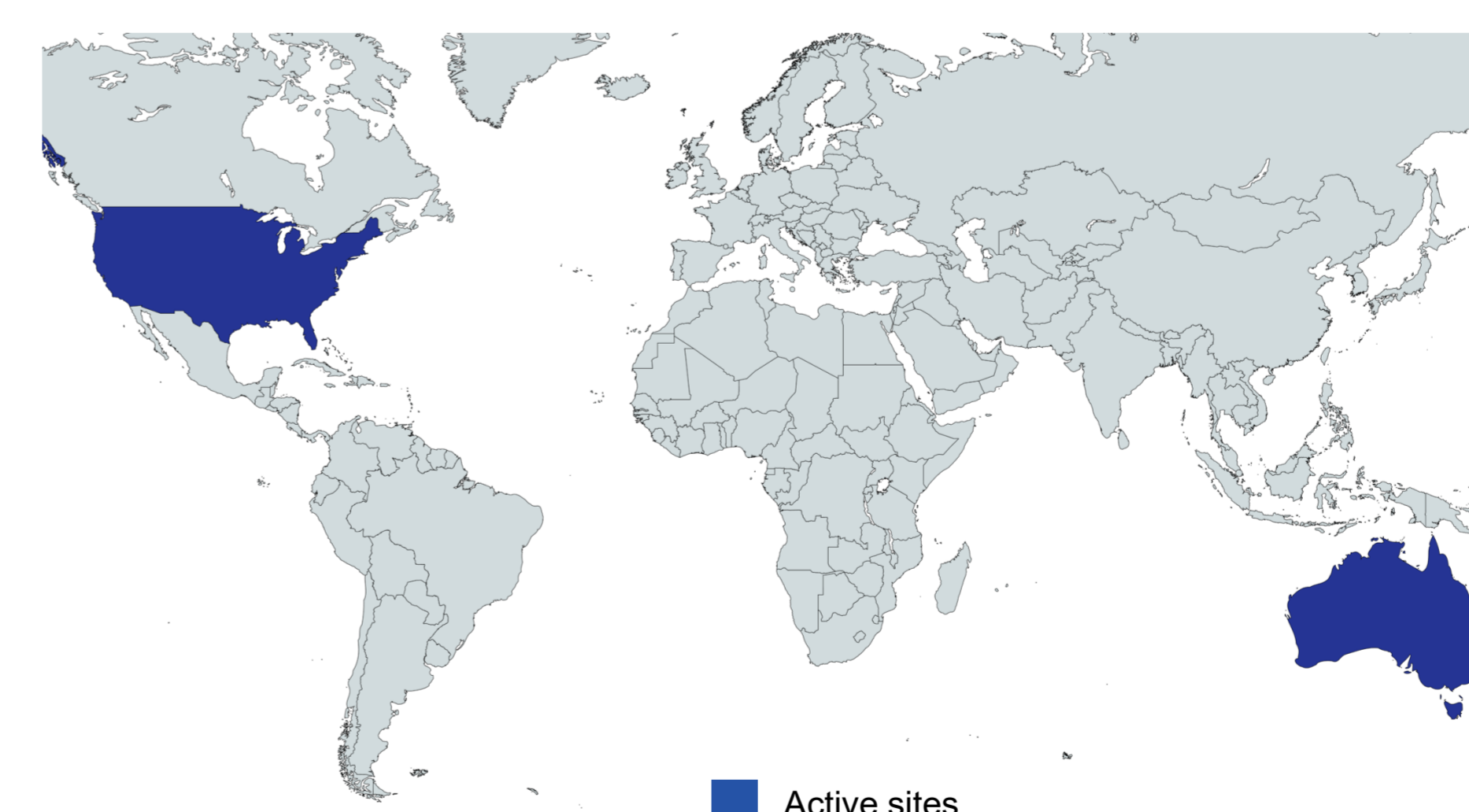
Key inclusion criteria

- For dose escalation or backfill: progressing from, intolerant to, or ineligible for (due to unavailability or contraindication) local standard of care therapies and have one of the following locally advanced or metastatic tumor types: hepatocellular carcinoma; biliary tract cancer; endometrial carcinoma; cervical cancer; ovarian cancer; gastric or gastroesophageal cancer; colorectal cancer; non-small cell lung cancer.
- Earlier-line participants, including those untreated in the advanced or metastatic setting, may also be eligible to participate in backfill cohorts.
- Tumor indication for dose optimization to be determined based on emerging CR-001 data.
- Life expectancy ≥ 3 months.
- ECOG PS score of 0–1.
- Adequate organ function and hematologic reserve based on laboratory parameters.
- Measurable disease defined by RECIST v1.1.
- For backfill and dose optimization: Willingness to provide recent archival tumor tissue sample or willingness to undergo biopsy.

Key exclusion criteria

- Malignancies other than disease under study within the past 3 years.
- History of prior Grade ≥ 3 immune-related AE on checkpoint inhibitor.
- History of drug-related pulmonary conditions, including Grade ≥ 2 pneumonitis, pulmonary fibrosis.

Planned patient population and current status



- Up to 290 patients are planned to be enrolled across the dose-escalation, tumor-specific backfill, and dose-optimization cohorts.
- This trial is currently enrolling in the US and Australia.
- Enrollment for global sites planned

CR-001
ClinicalTrials.gov
NCT07335497



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