ASCEND: A phase 1/2, dose-escalation, optimization, and dose-expansion study to evaluate the safety and antitumor activity of CR-001 in adults with locally advanced or metastatic solid tumors

Meredith Pelster[1], Amita Patnaik[2], Rebecca Kristeleit[3], Seung Tae Kim[4], Emily Putiri[5], Lindsey Granlund[5], Paul Herszdorfer[5], Bradley Sumrow[5], Min Lu[5], Ana Oaknin[6]

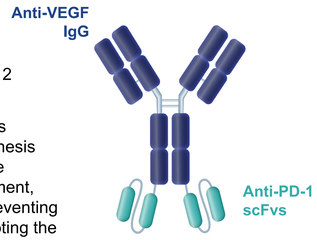
[1]Sarah Cannon Research Institute, Nashville, TN, USA; [2]The START Center for Cancer Research, San Antonio, Texas, USA; [3]Guy's and St. Thomas' NHS Foundation Trust, London, UK; [4]Samsung Medical Center, Seoul, Korea; [5]Crescent Biopharma, Waltham, MA, USA; [6]Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain

#TPS2693

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 as monotherapy and in combination with chemotherapy among patients with locally advanced or metastatic tumors.

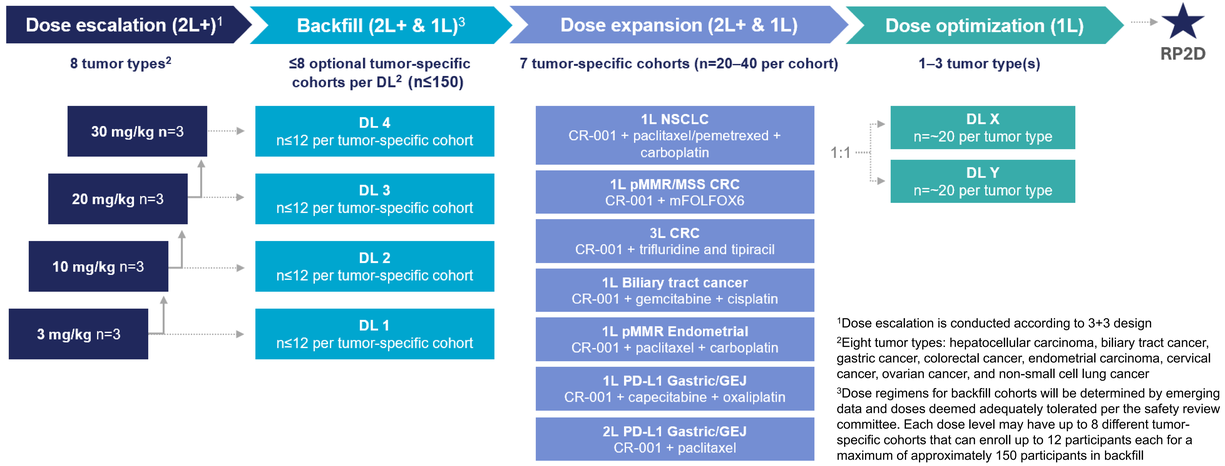
Figure 1. CR-001



Study design

- ASCEND (NCT07335497) is a global, first-in-human, open-label, phase 1/2 study evaluating CR-001 monotherapy and chemotherapy combinations 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 RP2D. Objectives and endpoints of the ASCEND study are detailed in the table opposite.
- The study consists of four parts: dose escalation, backfill, dose expansion, and dose optimization (**Figure 2**).
- Key inclusion/exclusion criteria are detailed on the right of the poster.

Figure 2. ASCEND study design



[1]Dose escalation is conducted according to 3+3 design
[2]Eight tumor types: hepatocellular carcinoma, biliary tract cancer, gastric cancer, colorectal cancer, endometrial carcinoma, cervical cancer, ovarian cancer, and non-small cell lung cancer
[3]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

Study objectives

Primary (all cohorts)
• Characterize the safety and tolerability of CR-001 as a single agent and in combination with chemotherapy in participants with locally advanced or metastatic solid tumors
Primary (part 3 – dose expansion)
• Characterize the preliminary antitumor activity of CR-001 in combination with chemotherapy by ORR
Secondary (all cohorts)
• 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
Secondary (dose escalation, backfill and dose optimization)
• Characterize the preliminary antitumor activity of CR-001
Secondary (dose expansion)
• Characterize the preliminary antitumor activity of CR-001 in combination with chemotherapy

Eligibility criteria

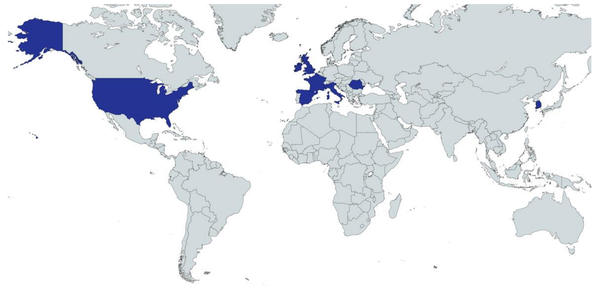
Key inclusion criteria

- For dose escalation or backfill only: progressing from, intolerant to, or ineligible for (due to unavailability or contraindication) local standard of care therapies and have and have locally advanced/metastatic disease of one of the tumor types listed in Fig 2.
- Earlier-line participants, including those untreated in the advanced or metastatic setting, may also be eligible to participate in backfill cohorts.
- 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, dose expansion, 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 adverse event on immunotherapy.
- History of drug-related pulmonary conditions, including Grade ≥2 pneumonitis, pulmonary fibrosis.

Active study sites and current status



- Up to 540 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, Ireland, Italy, Romania, South Korea, Spain, the UK and France.
- Further global expansion is planned.

CR-001
ClinicalTrials.gov
NCT07335497

Abbreviations

CRC, colorectal cancer; **DL**, dose level; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **GEJ**, gastroesophageal junction; **MSS**, microsatellite stable; **NSCLC**, non-small cell lung cancer; **ORR**, overall response rate; **PD**, pharmacodynamics; **PD-1**, programmed cell death-1; **PD-L1**, programmed death ligand-1; **PK**, pharmacokinetics; **pMMR**, proficient mismatch repair; **RECIST**, Response Evaluation Criteria in Solid Tumors; **RP2D**, recommended phase 2 dose; **VEGF**, vascular endothelial growth factor; **VEGFR2**, vascular endothelial growth factor receptor 2.

Acknowledgements

- The authors would like to thank all patients, their families, and investigators involved in the study.
- Protocol CR-001-101 is sponsored by Crescent Biopharma, Inc.
- Crescent Biopharma, Inc. funded the editorial/creative assistance for this poster, which was provided by Miller Medical Communications Ltd.