RESULTS FROM A PHASE 1 STUDY OF CDX-1140, A FULLY HUMAN ANTI-CD40 ANTAGONIST MONOCLONAL ANTIBODY (MAB), IN COMBINATION WITH PEMBROLIZUMAB

1Rachel Sanborn,2Nashat Gabrail,3Benedict Carneiro,4Mark O’Hara,5Rodolfo Bordini,6Michael Gordon,7Danny Khalil,8Ralph Hauke,9Cherie Taglienti,10Mark Rogalski,11Rachel Styles,12Diego Alvarado,13Deena Maurer,14Linda Creve,15Tibor Keler,16Michael Yelin.

1Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, United States; 2Gabrail Cancer Center, Canton, OH, United States; 3Lengorreta Cancer Center at Brown University, Lifespan Cancer Institute, Providence, RI, United States; 4Hospital of the University of Pennsylvania, Philadelphia, PA, United States; 5Georgia Cancer Specialists, Marietta, GA, United States; 6HonorHealth Research Institute, Scottsdale, AZ, United States; 7Memorial Sloan Kettering Cancer Center, New York, NY, United States; 8Nebraska Cancer Specialists, Omaha, NE, United States; 9Celldex Therapeutics, Inc., Hampton, NJ, United States

Background CD40 agonist mAbs can enhance the efficacy of checkpoint blockade in preclinical models and can functionally revive PD-1hi exhausted T cells. This Phase 1 study examined safety, clinical activity, and pharmacodynamics of CDX-1140 as monotherapy or in combination with other agents (NCT03329950). We now report the completed results from Part 3 of the study, combination with anti-PD-1 mAb pembrolizumab.

Methods Patients with advanced solid tumors and documented disease progression on a single prior anti-PD-1/L1 based regimen were enrolled. In dose-escalation (DE) cohorts, CDX-1140 was administered at 0.72 mg/kg and 1.5 mg/kg. Expansion cohorts (EX) in non-small cell lung cancer (NSCLC) and squamous cell carcinoma of head and neck (SCCHN) evaluated CDX-1140 1.5 mg/kg. Treatment was q3w co-administered with pembrolizumab 200 mg in both DE and EX.

Results 10 patients were treated in DE (renal cell carcinoma n=2, SCCHN n=2, n=1 for NSCLC, endometrial cancer, MSIhi-CRC, ocular melanoma, esophageal adenocarcinoma, MSIhi-cholangiocarcinoma) and 15 patients treated in EX; NSCLC (n=9) and SCCHN (n=6). The median number of prior regimens was 3. Treatment was generally well tolerated, with most treatment-related AEs (TRAE) being grade 1 or 2.

The most frequent TRAE at the CDX-1140 1.5 mg/kg dose level (n=21) were arthralgia (62%), fatigue (62%), nausea (48%), diarrhea (48%), vomiting (43%), myalgia (43%), fever (38%), chills (38%), AST increase (38%), bilirubin increase (24%), ALT increase (19%), and cytokine release syndrome (CRS) (19%). Across Part 3, there was 1 complete response (CR) in a patient with oropharyngeal cancer (HPV+ and PD-L1 status unknown); 9 additional patients had stable disease (SD), including 4 with SCCHN and 4 with NSCLC. The patient achieving CR received 4 prior regimens (including chemotherapy, pembrolizumab, and cetuximab), discontinued study therapy after 2 doses due to arthralgia (grade 3) and CRS (grade 2), and initially demonstrated a partial response that evolved into CR, with the response ongoing at 12+ months without further anti-tumor treatment. Of the 4 SCCHN with SD, 2 had target lesions shrinkage (-15% and -18%) and 2 had no change. One NSCLC patient had SD for 10+ months with a nadir in target lesions of -15%. Part 3 biomarker data will be presented.

Conclusions CDX-1140 in combination with pembrolizumab had an acceptable safety profile. Evidence of clinical benefit was most evident in patients with SCCHN, all of whom had progressive disease on prior anti-PD-1/L1 based therapies. Further studies are warranted.

Trial Registration NCT03329950

Ethics Approval The study was reviewed and approved by the following institutional review boards:

Providence Health & Services Institutional Review Board for Earle A. Chiles Research Institute/Providence Cancer Institute; approval number/ID: PHS IRB #201700532

WCG-IRB for Gabrail Cancer Center, Georgia Cancer Specialists, HonorHealth Research Institute, and Nebraska Cancer Specialists; approval number/ID: 20172645

Rhode Island Hospital IrKB#1 for Lengorreta Cancer Center at Brown University/Rhode Island Hospital/Lifespan Cancer Center; approval number/ID: LS-P-Camp

Office of Regulatory Affairs of the University of Pennsylvania for Hospital of the University of Pennsylvania; approval number/ID: UPCC 18917

Memorial Sloan Kettering Cancer Center Institutional Review Board/Privacy Board; approval number/ID: 18-225

Participants gave informed consent before taking part in the study.