A PHASE 1, OPEN-LABEL, DOSE ESCALATION AND EXPANSION STUDY OF CUE-102 MONOTHERAPY IN HLA-A*0201 POSITIVE PATIENTS WITH WT1-POSITIVE RECURRENT/METASTATIC CANCERS

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Background Immuno-STATs™ are modular fusion proteins designed for the selective activation of tumor-antigen specific CD8+ T cells. CUE-102, the second Immuno-STAT in clinical trials, is composed of a human leukocyte antigen (HLA) complex, HLA-A*0201, a peptide epitope derived from the Wilms Tumor 1 (WT1) protein, and 4 molecules of reduced affinity human interleukin-2 (IL-2), and is designed to bind, expand, and activate WT1-specific CD8+ T cells for the treatment of WT1-positive cancers. In pre-clinical studies, CUE-102 elicits selective expansion of WT1-specific cytotoxic CD8+ T-cells in vitro and in vivo.1

Methods CUE-102-01 is a phase 1, open-label, 2-part, multi-center study evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and preliminary antitumor activity of CUE-102 monotherapy administered every three weeks in HLA-A*0201 positive patients with WT1 positive recurrent/metastatic Colorectal, Gastric/Gastroesophageal Junction (GEJ), Pancreatic and Ovarian cancer who have failed conventional therapies. Part A is a dose escalation phase following 3+3 design rules with a Bayesian Logistic Regression Model (BLRM) overlay. Dose levels that exhibit an immune response may be expanded to further characterize activity and toxicity. Part B is a dose expansion/confirmation phase in patients with colorectal cancer.

The primary objectives of Part A are to evaluate dose-limiting toxicities and maximum tolerated dose during the first cycle of treatment, to evaluate the pharmacokinetics (PK) of CUE-102, and to establish a recommended Phase 2 dose. Secondary objectives of Parts A and B include evaluating the safety and tolerability of CUE-102 using NCICTCAE v5.0; preliminary antitumor activity by RECIST 1.1 including objective response rate (ORR), duration of response (DOR), durable stable disease (DSD) (SD ≥ 6 weeks), clinical benefit rate (CBR), progression-free survival (PFS); overall survival (OS); the potential for CUE-102 mediated immune response; and the potential immunogenicity of CUE-102. Exploratory objectives include evaluation of biomarkers of activity and immune effects, and preliminary antitumor activity by iRECIST.

Eligible patients must have locally advanced/nonresectable or metastatic disease, an ECOG status of 0 or 1, life expectancy > 12 weeks and measurable disease by RECIST 1.1 criteria. Patients with colorectal and cisplatin-sensitive ovarian cancer must have documented disease progression to 2 prior systemic treatment regimens (CUE-102 will be ≥ 3rd line therapy); patients with Gastric/GEJ, pancreatic and cisplatin-resistant ovarian cancer must have documented disease progression to 1 prior systemic treatment regimens (CUE-102 will be ≥ 2nd line therapy).

Results Trial is currently open and enrolling as of June 14, 2022.

Acknowledgements The authors would like to thank all the patients who are participating in this study. The study is sponsored by Cue Biopharma.

Trial Registration ClinicalTrials.gov NCT05360680

REFERENCE

Ethics Approval This study was approved by Ethics and Institutional Review Boards (IRBs) at all study sites. IRB reference numbers: WIRB 1331836 (Carolina BioOncology), WIRB 1335388 (Gabrail Cancer Center)