A phase 1 dose-escalation and expansion study of CUE-101, a novel HPV16 E7-pHLA-IL2-Fc fusion protein, given as monotherapy and in combination with pembrolizumab in patients with recurrent/metastatic HPV16+ head and neck cancer.

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Background and Study Design

- **Immuno-STATs**™ (ISTs) are TCR-selective engager biologics comprised of a bivalent peptide-MHC complex and multivalent co-agonitory molecules built on an Fc framework to enable stability, valency, favorable PK, and manufacturability.
- The CUE-100 series ISTs are designed to deliver attenuated interleukin-2 (IL-2) selectively to tumor-specific CD8+ T cells [1].
- **CUE-101**, the first IST in clinical trials, is composed of an HLA-A*0201 complex, a peptide epitope derived from the HPV-16 E7 protein, and 4 molecules of reduced affinity IL-2 that is designed to limit, expand, and activate HPV-16 specific CD8+ T cells for the treatment of HPV+ cancers when given intravenously (IV) every 3 weeks (Q3W).
- **CUE-101-01** (NCT03979788) is a Phase 1, open, dose escalation and expansion study in HLA-A*0201 positive patients with HPV16+ recurrent/metastatic head and neck cancer (RM HNSCC).

Patient Demographics & Prior Therapies

- Patients with RM HNSCC that progressed following platinum or checkpoint inhibitor-based therapies are eligible for CUE-101 monotherapy. Eligibility for RM HNSCC patients also include patients with prior pembrolizumab therapy.

Adverse Events All Patients (Monotherapy and Combination)

- **Time on Treatment (weeks)**
- **Time to Systolic follow-up (months)**

Best Overall Response in Combination Patients at the RP2D

- Overall survival (months) in patients treated with 4 mg/kg CUE-101 (N=16), from time of first dose of drug as of 12-Apr-2023.

Change in HPV16 cDNA in Combination Patients at the RP2D

- Overall survival (months) in patients treated with 4 mg/kg CUE-101 plus pembrolizumab (N=16), from time of first dose of drug as of 12-Apr-2023.

Summary

- Forty-nine (49) patients were treated with CUE-101 monotherapy at doses ranging from 0.06 to 8 mg/kg and a maximum tolerated dose (MTD) was not established. The 4 mg/kg cohort was expanded to 20 patients.
- Twenty-two (22) patients were treated with CUE-101 at doses ranging from 1 to 4 mg/kg in combination with 200 mg pembrolizumab and no dose-limiting toxicity (DLT) was observed. The 4 mg/kg pembrolizumab dose was chosen for expansion and enrollment to a total of 20 patients.

Temporal Changes in Tumor Burden in Combination Patients at the RP2D

- Onset and duration of response are indicated on the plot. Kaplan-Meier estimate of median PFS 4.9 months [95% CI; 2.5, NA].
- ADAs following CUE-101 monotherapy occur transiently, decreasing over time in all patients with confirmed ADAs and generally do not persist throughout a patient’s treatment course.
- Unanticipated, significant safety concerns have emerged, and AEs have been readily managed with appropriate care in the clinical setting.
- ADAs following CUE-101 monotherapy occur transiently, decreasing over time in all patients with confirmed ADAs and generally do not persist throughout a patient’s treatment course.
- Overall survival in patients treated at the monotherapy RP2D continues to mature, Kaplan-Meier estimate of median OS 22.4 months (95% CI; 17.6, NA). Many thanks also to the investigators and study personnel for their hard work in support of this study. This study is sponsored by Cue Biopharma, Inc. and conducted in collaboration with UCSF, in support of the study. The study is sponsored by Cue Biopharma Inc. and conducted in collaboration with UCSF. Core study contributors include S. N. Quayle, N. Girgis, D. R. Thapa, et al. The authors would like to thank all the patients participating in this trial as well as their families and caregivers.