Background Immuno-STATs™ are novel, modular fusion proteins designed to selectively activate tumor-antigen-specific CD8+ T cells. CUE-101 is comprised of a human leukocyte antigen (HLA) complex, HLA-A*0201, a peptide epitope derived from the HPV16 E7 protein, and 4 molecules of a HLA-IL2-FC fusion protein, enhances tumor antigen specific T cell activation for the treatment of HPV16-driven malignancies. Clin Cancer Res 2020;26:1953–64.

Methods CUE-101-01 is a first-in-human study in HLA-A*0201 positive patients with HPV16+ recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). Safety of escalating monotherapy and combination doses was evaluated to establish the recommended phase 2 dose (RP2D) for expanded enrollment. Patients with R/M HNSCC refractory to 1 or more prior platinum or pembrolizumab based systemic treatments received CUE-101 monotherapy, and patients with R/M HNSCC and PD-L1 tumor expression received combination CUE-101 and 200 mg pembrolizumab as first line treatment. Study treatment was administered intravenously every 3 weeks until progression or toxicity. Objectives included evaluation of safety, pharmacokinetics (PK), pharmacodynamics (PD), and antitumor activity.

Results As of June 30, 2021, 39 patients have received CUE-101 monotherapy ranging from 0.06 to 8 mg/kg. The maximum tolerated dose (MTD) was not identified. Based on PK, PD and clinical data, a monotherapy RP2D of 4 mg/kg was selected. The combination cohort of 1 mg/kg CUE-101 and pembrolizumab has been tested and dose escalation is ongoing. Adverse events have included CTCAE grade 2 or less fatigue (41%), anemia (31%), lymphopenia (24%), chills (21%), decreased appetite (19%) and dyspnea (17%). CUE-101 PK data demonstrate dose-dependent increases in drug exposure that are sustained upon repeat dosing. PD data demonstrate dose-dependent expansion of HPV-16 E711-20-specific CD8+ T cells, sustained increase in natural killer cells and transient increase in Treg cells. An increase in CD3+ GZMB+ tumor infiltrating T cells was observed in tissue following treatment with CUE-101 in one patient with available pre- and post-treatment biopsies. One patient at the CUE-101 monotherapy RP2D has an ongoing partial response and 8 of 33 patients have experienced stable disease ≥ 12 weeks based on RECIST 1.1 criteria.