A PHASE 2 STUDY OF EVORPACEPT (ALX148) IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC); ASPEN-03

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Background Both innate and adaptive immune responses are important components of anticancer immunity. CD47 is a marker of self that interacts with SIRP α on myeloid immune cells, inhibiting their function. CD47 is upregulated by tumors to evade immune responses and its expression is associated with poor prognosis. Evorpaccept is a high affinity CD47-blocking fusion protein with an inactive Fc region designed to be safely combined with and to enhance the efficacy of standard anticancer therapeutics. Evorpaccept used in combination with pembrolizumab has the potential to augment both innate and adaptive anti-tumor immune responses. As an antibody inhibiting PD-1/PD-L1 signaling in the T cell immune checkpoint, pembrolizumab has demonstrated anti-tumor efficacy through activation of tumor-infiltrating lymphocytes. Pembrolizumab as a single agent is a standard treatment option for patients with previously untreated recurrent or metastatic (R/M) HNSCC with PD-L1-positive (combined positive score [CPS] ≥ 1) tumors. The combination of evorpaccept + pembrolizumab has shown preliminary efficacy and acceptable tolerability in initial results available from the cohort of patients with ≥ 2 nd line advanced HNSCC in the ongoing Phase 1 ASPEN-01 study.¹ PD-L1-unselected patients who had not received prior checkpoint inhibitor treatment were treated with evorpaccept + pembrolizumab and experienced a 40% ORR and 4.6 months median PFS, comparing favorably with historical controls. Based on these encouraging results, the ASPEN-03 study will assess the efficacy and safety of evorpaccept in combination with pembrolizumab in previously untreated patients with metastatic or unresectable recurrent PD-L1 positive HNSCC.

Methods ASPEN-03 (figure 1) is an ongoing non-comparative, open-label, randomized Phase 2 global study of evorpaccept + pembrolizumab or pembrolizumab alone in patients with metastatic or unresectable recurrent, PD-L1-positive (CPS ≥ 1) HNSCC who have not yet been treated for their advanced disease. After an initial safety lead-in cohort, ~105 patients will be randomized 2:1 to receive evorpaccept + pembrolizumab or pembrolizumab alone. Minimization factors used to randomize patients include geography, CPS, and HPV (p16) status. Patients in the evorpaccept + pembrolizumab treatment arm will receive evorpaccept 45 mg/kg IV Q3W. All patients will receive pembrolizumab 200 mg IV Q3W (maximum of 35 cycles). The primary endpoint in this Simon two-stage trial design is objective response rate using RECIST v1.1. Key secondary endpoints include duration of response, progression-free survival, overall survival, and safety. Exploratory endpoints will characterize pharmacodynamic properties.

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Trial Registration ClinicalTrials.gov identifier, NCT04675294

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Ethics Approval The study was approved by all participating institutions' Ethics and/or Review Boards.

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