656 ELI-002 IMMUNOTHERAPY INDUCES BROAD POLYFUNCTIONAL T CELL RESPONSES IN SUBJECTS WITH HIGH RELAPSE RISK KRAS MUTATED PANCREATIC DUCTAL ADENOCARCINOMA AND COLORECTAL CANCER

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Background Successful advancement of vaccine strategies for the treatment of solid tumors has been limited due to the limitations of vaccine delivery platforms and inadequate immune responses. ELI-002 immunotherapy uses Amphiphile (Amph) lymph node targeting to improve the potency of vaccination. Amph-modification promotes lipid-mediated binding to albumin resulting in delivery of antigen/adjuvant to lymph nodes where uptake by antigen-presenting cells leads to effective T cell activation. Kirsten rat sarcoma (KRAS) is mutated in one-quarter of human solid tumors, including approximately 90% of pancreatic ductal adenocarcinoma (PDAC) and 50% of colorectal cancer (CRC), making it an attractive target for lymph node-targeted immunotherapy using the Amph platform. ELI-002 2P was well tolerated, and 77% of patients exhibited biomarker response including 32% who exhibited circulating tumor DNA (ctDNA) clearance.

Methods ELI-002–001 is a first-in-human Phase 1 trial of ELI-002 2P immunotherapy as adjuvant treatment for subjects with high relapse-risk mutant KRAS (mKRAS) PDAC and CRC. ELI-002 2P consists of 2 Amph-modified mKRAS peptide antigens, Amph-G12D and Amph-G12R (Amph-Peptides 2P), and a Amph-modified immune-stimulatory oligonucleotide adjuvant (Amph-CpG-7909). 25 subjects were randomized to receive ELI-002 2P at 1.4 mg of Amph-Peptides 2P and Amph-CpG-7909 at 5 dose levels; 0.1, 0.5, 2.5, 5, and 10 mg. Peripheral blood was collected longitudinally to assess specificity, polyfunctionality, and phenotype of mKRAS-specific T cells.

Results 87% of evaluable subjects (20/23) induced mKRAS-specific T-cells post-vaccination as assessed by direct ex vivo Fluorospot and/or ICS assays with an average 56-fold increase from baseline. Further, a balanced $CD4^+$ and $CD8^+$ T cell response was observed in 50% of subjects and a majority were central and effector memory T cells. Evaluation of the breadth of responses to 7 different KRAS mutations revealed broad cross-reactivity to KRAS mutants including non-immunizing epitopes and low responses to WT. A high frequency of polyfunctional cells secreting IFNγ, TNFα, IL-2, and/or Granzyme B was observed. Additional phenotypic and functional analysis of mKRAS-specific T cells is ongoing.

Conclusions ELI-002 induces robust and broadly reactive mKRAS-specific T cell responses in most subjects (87%) at high risk for relapse. This off-the-shelf lymph node-targeted vaccine has many advantages including high immunogenicity yielding balanced $CD4^+$ and $CD8^+$ T cell responses targeting vaccine antigens that are critical for tumor survival. A Phase 1/2 clinical trial investigating a new 7 peptide formulation, ELI-002 7P (G12D, R, V, A, C, S, G13D; NCT NCT05726864), is currently in progress.

Trial Registration NCT04853017

Ethics Approval The study was approved by the local institutional review board at each study site and the US FDA. All patients provided written and informed consent.