ELI-002 Immunotherapy Induces Broad Polyfunctional T cell Responses in Subjects with High Relapse Risk KRAS Mutated Pancreatic Ductal Adenocarcinoma and Colorectal Cancer

James R. Perry[1], Lochana M. Seenappa[1], Haley VanWyk[1], Amy M. Tavares[1], Thian Kheoh[1], Esther Welkowsky[1], Christopher M. Haqq[1], Peter C. DeMuth[1], and Lisa K. McNeil[1]

[1] Elicio Therapeutics, Inc. 451 D St., Ste 501, Boston, MA 02210

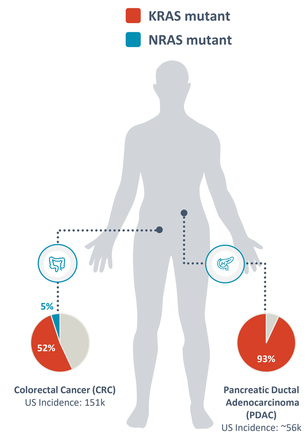
Why Target mutated KRAS with Therapeutic Vaccination?

1 Mutant KRAS Drives 25% of Solid Human Cancers

- **Prevalent** among numerous tumor types[1-2]
- Overall **poor clinical prognosis**[3]
- **Limited therapeutic options**

2 Mutant KRAS is a Promising Tumor Antigen

- **Truncal**: mutations occur early, expressed uniformly in all tumor cells
- **Driver**: mKRAS signaling is required for tumor growth and survival
- **Highly prevalent**: involved in ~25% of solid tumors[1-2]
- **Public neoantigen**: not centrally tolerized, cognate TCRs present in naïve repertoire[4-5]
- **Promiscuous HLA presentation**: potential off-the-shelf use in diverse patient population[6-8]
- **Proven Clinical MOA**: mKRAS-specific T cells known to mediate anti-tumor efficacy[4-5]
- **Multi-targeting potential**: recognition of clonal and subclonal mKRAS variants to prevent escape[9]



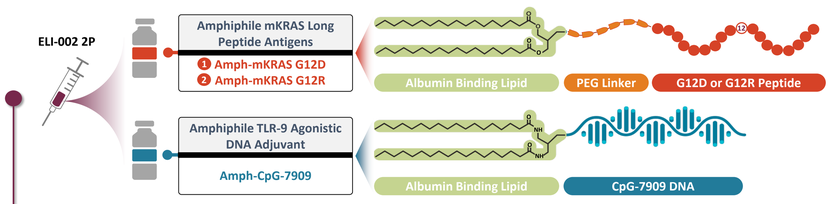
ELI-002 2P: Advancing Innovation for mKRAS Cancer Vaccines

1 Technological Innovation: Amphiphile Lymph Node Targeting Platform[10-11]

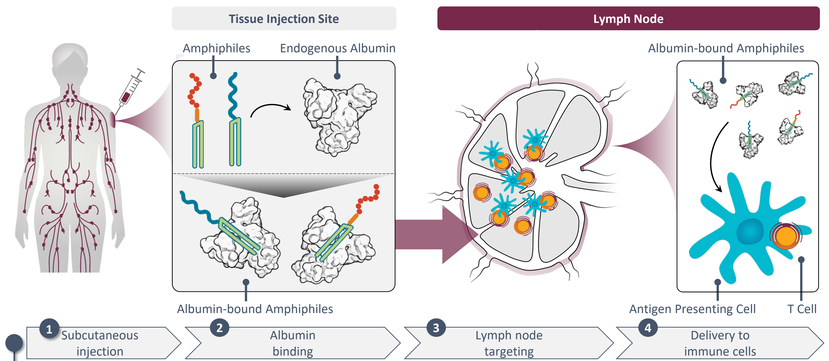
- **Smart trafficking to the lymph nodes** after subcutaneous dosing generates immune responses with increased magnitude, function, and durability.
- **Takes advantage of potent lymph node immune mechanisms**, including activation of innate and adaptive cells, antigen-spreading, and improved tumor T cell trafficking / infiltration.
- Mutant KRAS peptides provide a **validated antigen** for application of the Amphiphile platform.
- Lymph node delivery of potent adjuvants **minimizes systemic exposure to improve safety.**

2 Clinical Innovation: Treatment in High Relapse-Risk Adjuvant Setting

- Targeting surgically debulked tumors **enables T cells to address minimal residual disease to potentially eliminate** remaining tumor cells and protect against recurrence.
- Activating the immune system **before loss of HLA expression** in the tumor microenvironment in a chemotherapy-free window of opportunity.
- Other oncology vaccines have typically been used in later lines of therapy for advanced disease, **after onset of tumor immune resistance.**
- In the adjuvant setting, **tumor biomarkers (ctDNA, serum tumor antigen) are early predictors of disease control or recurrence.**

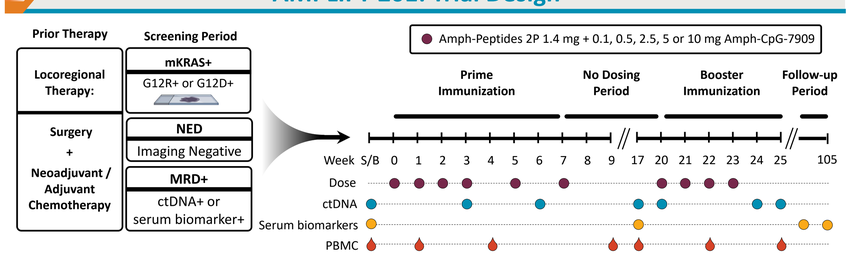


- Inclusion of **18-mer G12D and G12R mKRAS peptides** allows for delivery of **diverse HLA I and II – restricted epitopes** for presentation on varied patient HLA molecules.
- **Amphiphile (Amph)-modification of peptides** promotes binding to endogenous albumin at the injection site to promote collection in lymphatic vessels for **lymph node delivery**, and prevents peptide uptake into local capillaries avoiding delivery to irrelevant or tolerogenic sites.
- **Amph-CpG-7909 provides** potent immune activation via TLR-9 stimulation of lymph node-resident professional antigen presenting dendritic and other key immune cells.



- **Conventional vaccine components** (e.g. peptide antigens and molecular adjuvants) are rapidly absorbed into blood capillaries after administration leading to **poor delivery to lymph nodes where protective immune responses are orchestrated.**
- **Amph-modification promotes albumin binding to reprogram vaccines for enhanced lymph node delivery** resulting in coordinated transport of antigen and adjuvant to immune cells. Improved uptake by Antigen Presenting Cells results in enhanced **antigen-presentation and co-stimulation to cognate T cells.**
- Restricted delivery to lymph nodes **minimizes systemic exposure to avoid toxic effects of potent adjuvants.**

AMPLIFY 201: Trial Design[12]



Patients

Safety

Baseline Characteristics: 20 Pancreatic (PDAC), 5 Colorectal (CRC) were evaluated for safety as of data cutoff: April 25, 2023

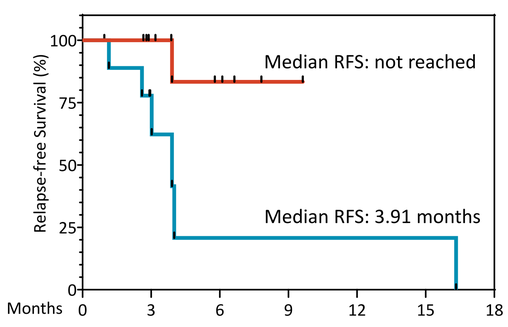
Safety: **No TEAEs ≥ Grade 3, no Dose Limiting Toxicities, no Cytokine Release Syndrome observed across all dose levels; 44% had Grade 1-2 TEAEs: e.g. injection site reaction, fatigue, headache, nausea**[12]

AMPLIFY 201: Immunogenicity Methods

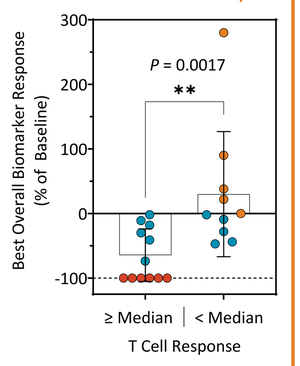
- **Immunogenicity of ELI-002 2P** was assessed using longitudinally collected peripheral blood from 23 evaluable patients to assess specificity, polyfunctionality, antigen breadth, and phenotype of mKRAS-specific T cells.
- PBMCs from each patient were individually stimulated with overlapping peptides for each of the seven mKRAS antigens (G12R, G12D, G12V, G12C, G12A, G12S and G13D) and the WT antigen, for evaluation of mKRAS-specific T cell responses using both **direct *ex vivo*** and ***in vitro* stimulated** assays.
- **T cell responses** and **polyfunctionality** were determined by a direct *ex vivo* IFNγ/Granzyme B (GrB) Fluorospot and a 10-day *in vitro* stimulated (IVS) IFNγ/TNFα Fluorospot assay, where a positive immune response was defined as >2-fold over baseline and at least 50 SFC per million PBMCs.
- **Polyfunctionality** and **phenotype** of patient T cells were further characterized using an *ex vivo* and IVS intracellular cytokine staining (ICS) assay, where responder populations were defined as >2-fold over baseline and a frequency of at least 0.1% Cytokine$^+$. The ICS assay included markers for CD3, CD4, CD8, Memory (CCR7, CD45RA, CD45RO), cytokines (IFNγ, TNFα, IL2), cytolysis (GrB, Perforin, CD107a), activation markers (CD69, CD137, CD154), and proliferation (Ki67).

mKRAS T Cell Responses Correlate with Reduction in Risk of Relapse or Death[13]

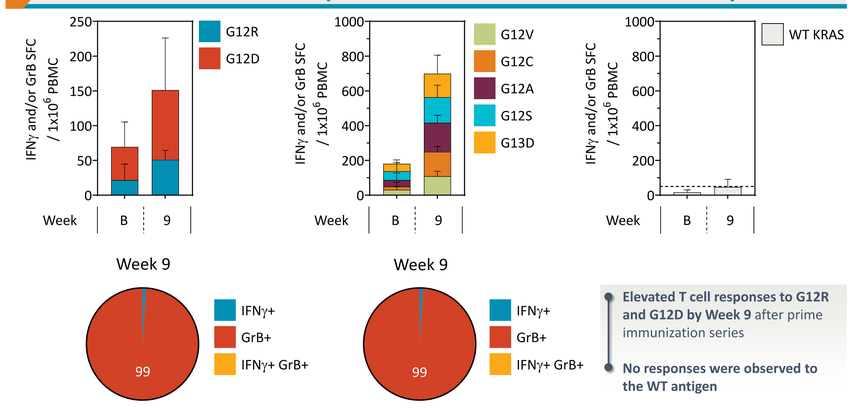
Strength of T Cell Response ➤ 86% Reduced Risk of Relapse or Death



Tumor Biomarker Response

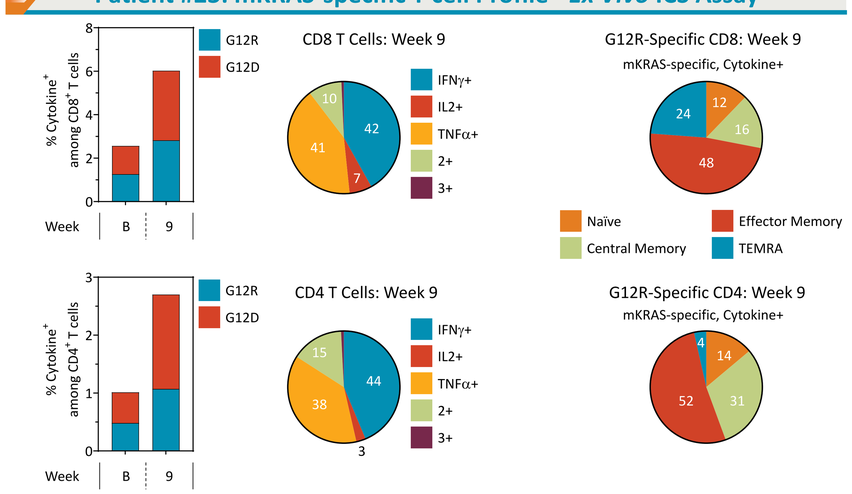


Patient #23: mKRAS-specific T cell Profile - *Ex Vivo* Fluorospot

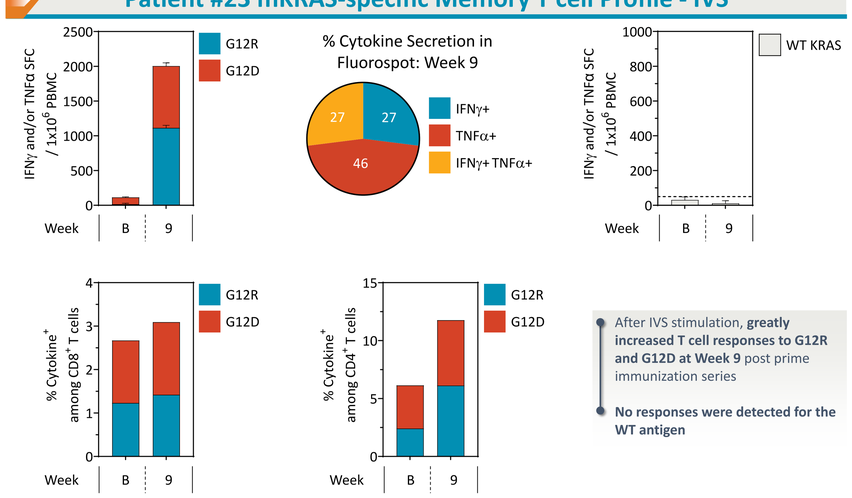


- **Elevated T cell responses to G12R and G12D by Week 9** after prime immunization series
- **No responses were observed to the WT antigen**

Patient #23: mKRAS-specific T cell Profile - *Ex Vivo* ICS Assay

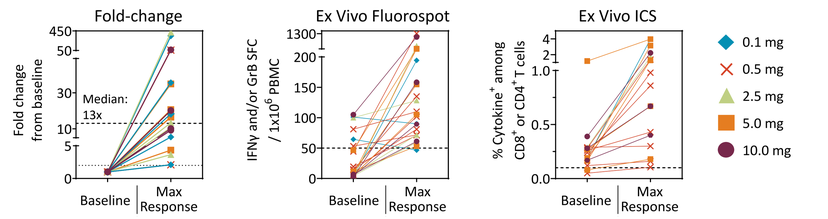


Patient #23 mKRAS-specific Memory T cell Profile - IVS

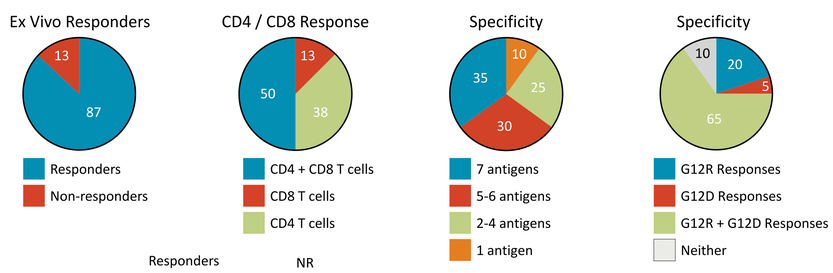


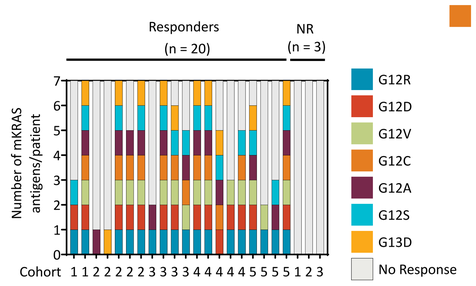
- After IVS stimulation, **greatly increased T cell responses to G12R and G12D at Week 9** post prime immunization series
- **No responses were detected for the WT antigen**

Expansion of mKRAS-specific T cells by ELI-002 2P Immunization



- **87% of Patients generated direct ex vivo detectable mKRAS-specific T cell responses** following ELI-002 2P Immunization, with **100% Responders at the highest dose levels** (5.0 and 10.0 mg)

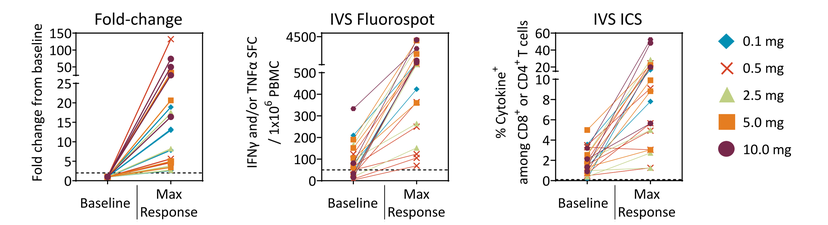




Amph-CpG Dose Level	*ex vivo* T cell response (n, %)	Average fold-change
0.1 mg	2/3 (67%)	30
0.5 mg	5/6 (83%)	82
2.5 mg	4/5 (80%)	113
5.0 mg	5/5 (100%)	19
10.0 mg	4/4 (100%)	26
Total	20/23 (87%)	56

- **CD4 and CD8 T cell responses were observed**, with 50% generating mixed CD4 + CD8 responses
- mKRAS-specific **T cells were polyfunctional** (IFNγ, TNFα, IL-2), **specific to both immunizing and non-immunizing mKRAS antigens**

Increased mKRAS-specific Memory T cells Assessed by IVS



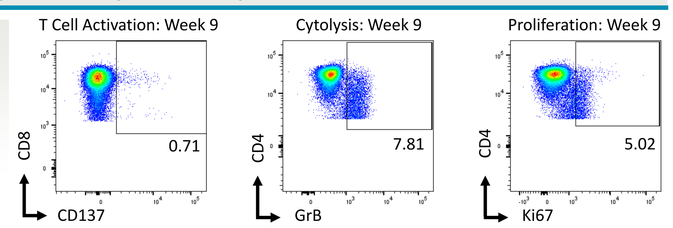
- **100% of patients induce mKRAS-specific memory T cell responses** after *in vitro* stimulation

Increased Polyfunctionality of mKRAS-specific T cells after ELI-002 2P Immunization

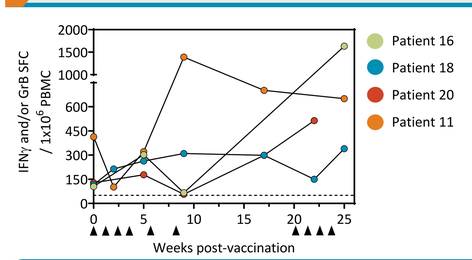
Patient #23

Polyfunctional T cell Profile:

Increased activation, cytolysis, and proliferation after vaccination



ELI-002 2P Immunization Elicits Durable mKRAS-specific Immune Responses



- **ELI-002 2P vaccination generates long-lasting mKRAS-specific T cell responses**
- **100% (4/4) of evaluable patients maintain elevated T cell responses** above baseline post-boost immunization
- **An increased post-boost T cell response was observed in 75% (3/4) of evaluable patients** compared to pre-boost T cell levels

TAKE HOME MESSAGES

T Cell Response MOA Correlated to:

- ➤ **86% Reduced Risk of Relapse or Death**
- ➤ **Tumor Biomarker Response**

Lymph node-targeted Therapeutic mKRAS-specific Cancer Vaccine ELI-002 2P:

- ➤ Direct *ex vivo* mKRAS-specific T cell responses observed in **87%** of patients and IVS responses were observed in **100%** of patients
- ➤ **50%** of patients generated both CD4 and CD8 T cell responses
- ➤ T cells exhibited robust functional quality: activation, cytokine production, cytolytic capacity, proliferation, memory phenotype
- ➤ **100%** (4/4) of patients evaluable for durability maintained elevated T cell responses above baseline

✓ **Phase 1, randomized Phase 2 Study of ELI-002 7P (NCT05726864) in PDAC patients: targeting G12D, R, V, C, A, S, G13D**

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Acknowledgements

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