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AMPLIFY-7P, a first in human safety and efficacy trial of adjuvant mKRAS-specific lymph node-targeted Amphiphile ELI-002 7P vaccine in minimal residual disease positive pancreatic and colorectal cancer patients

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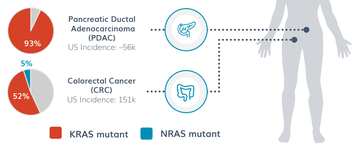
Why Target mutated KRAS with Therapeutic Vaccination?

1 Mutant KRAS Drives 25% of Solid Human Cancers

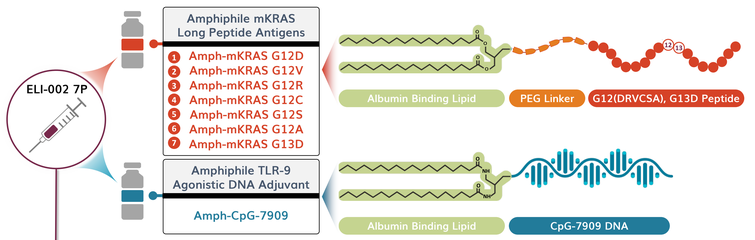
- **Prevalent** among numerous tumor types[1-2]
- Overall **poor clinical prognosis**[3]
- **Limited therapeutic options**



2 Mutant KRAS is a Promising Tumor Antigen

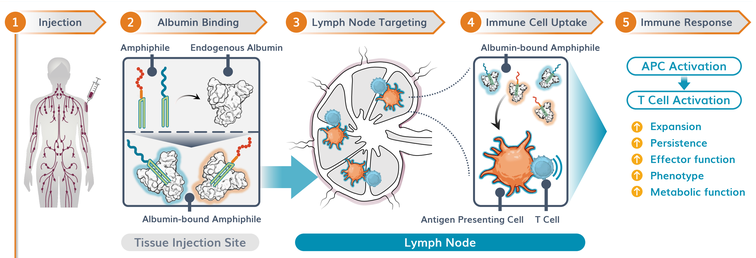
- **Truncal**: mutations occur early, expressed uniformly in all tumor cells
- **Driver**: mKRAS signaling is required for tumor growth and survival
- **Highly prevalent**: involved in ~25% of solid tumors[1-2]
- **Public neoantigen**: not centrally tolerized, cognate TCRs present in naive repertoire[4-5]
- **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]

Designing a Therapeutic Vaccine Targeting mKRAS: ELI-002 7P



- Inclusion of **18-mer G12X and G13X mKRAS peptides** allows for delivery of **diverse HLA I and II–restricted epitopes** for presentation on various patient HLAs
- **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

The AMP-Platform: Enhanced Lymph Node Delivery



- **Smart trafficking to the lymph nodes** after subcutaneous dosing generates immune responses with increased magnitude, function, and durability [10,11].
- **Takes advantage of potent lymph node immune mechanisms**, including activation of innate and adaptive immune cells, antigen-spreading, and improved tumor T cell trafficking / infiltration.
- Mutant KRAS peptides provide **validated antigens** for application of the Amphiphile platform.
- Lymph node delivery of potent adjuvants **minimizes systemic exposure to improve safety.**

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- For author disclosures please refer to the abstract.

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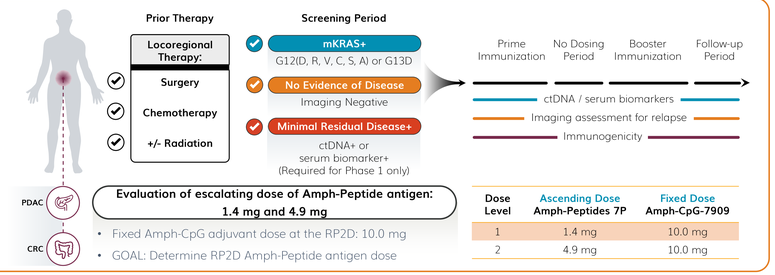
elicio THERAPEUTICS

AMPLIFY-7P: Prevention of Relapse in High-risk PDAC and CRC

Phase 1 Schema



Evaluation of escalating dose of Amph-Peptide antigen: 1.4 mg and 4.9 mg

- Fixed Amph-CpG adjuvant dose at the RP2D: 10.0 mg
- GOAL: Determine RP2D Amph-Peptide antigen dose

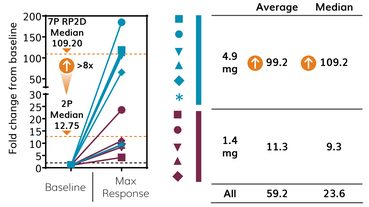
Dose Level	Ascending Dose Amph-Peptides 7P	Fixed Dose Amph-CpG-7909
1	1.4 mg	10.0 mg
2	4.9 mg	10.0 mg

mKRAS-specific T Cell Responses Increased >8x at RP2D 4.9 mg vs 1.4 mg

Cell Response [a]

AMPLIFY-7P mKRAS-specific T Cell Fold-Changes by Dose Level

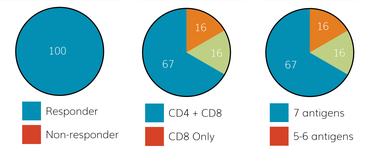
Direct Ex Vivo T Cell Response | 7P Dose | T Cell Response



	Average	Median
4.9 mg	99.2	109.2
1.4 mg	11.3	9.3
All	59.2	23.6

AMPLIFY-7P mKRAS-specific T Cell Response: 4.9 mg Antigen Dose

mKRAS T Cell Response | CD4 / CD8 Response | mKRAS Specificity



ELI-002 2P vs 7P	ELI-002 2P [12]	ELI-002 7P (All)	ELI-002 7P (4.9 mg)
T Cell Response Rate	84%	100%	100%
Median Fold Change	12.75	23.6	109.2
% CD4 + CD8 T cells	59.0%	63.6%	66.7%
Response to 7 mKRAS Antigens	52.4%	**45.5%**	**66.7%**

ELI-002 7P RP2D 4.9 mg induces enhanced mKRAS-specific T cell response compared to ELI-002-2P:

- 100% Ex vivo T cell response based on Fluorospot and ICS
- >8x Improved median T cell fold-change (109.2 vs 12.75)
- 66.7% CD4 and CD8 T cell response
- 66.7% with T cell response targeting 7/7 mKRAS antigens

- **Immunogenicity of ELI-002 7P** was assessed from 11 evaluable patients: PBMCs were individually stimulated with overlapping peptides for each of the mKRAS antigens (G12D, V, R, C, A, S, G13D) to assess mKRAS specificity, T cell polyfunctionality, and breadth of mKRAS response.
- **T cell responses** and **polyfunctionality** were determined by a direct *ex vivo* IFNγ/Granzyme B Fluorospot (positive response was defined as >2-fold over baseline, >50 SFC per million PBMCs) and *ex vivo* IFNγ/TNFα/IL2 ICS assay (positive response was defined as >2-fold over baseline, >0.1% Cytokine+).

[a] Measured among 11 evaluable patients as of the data cut off: December 18, 2023

Demographics and Baseline Characteristics

Amph-Peptide 7P Dose	1.4 mg n=6	4.9 mg n=8	Overall n=14
Age (years)			
Median	67.5	72.5	70.5
Range	38-76	55-75	38-76
Female Sex, n (%)	4 (66.7)	4 (50.0)	8 (57.1)
Race, n (%)			
Asian	1 (16.7)	0	1 (7.1)
White	4 (66.7)	7 (87.5)	11 (78.6)
Not reported	1 (16.7)	1 (12.5)	2 (14.3)
ECOG PS, n (%)			
0	5 (83.3)	6 (75.0)	11 (78.6)
1	1 (16.7)	2 (25.0)	3 (21.4)
Disease Diagnosis, n (%)			
PDAC	5 (83.3)	8 (100)	13 (92.9)
CRC	1 (16.7)	0	1 (7.1)
Disease Stage at Screening			
Stage I, II	4 (66.7)	3 (37.5)	7 (50.0)
Stage III	2 (33.3)	5 (62.5)	7 (50.0)
Prior Anti-cancer:			
Chemotherapy	6 (100)	8 (100)	14 (100)
Surgery	6 (100)	8 (100)	14 (100)
Radiation therapy	0	4 (50.0)	4 (28.6)

ECOG: Eastern Cooperative Oncology Group; PS: performance stats

Adverse Events and Patient Summary

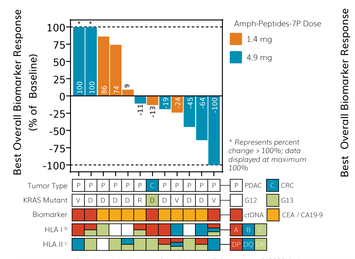
Amph-Peptide 7P Dose	1.4 mg n=6	4.9 mg n=8	Overall n=14
Adverse Event Term [a]			
Patients with Any Related TEAE, n (%)	5 (83.3)	6 (75.0)	11 (78.6)
Fatigue	3 (50.0)	3 (37.5)	6 (42.9)
Malaise	1 (16.7)	2 (25.0)	3 (21.4)
Diarrhea	1 (16.7)	2 (25.0)	3 (21.4)
Abdominal Distension	2 (33.3)	0	2 (14.3)
Abdominal Pain	1 (16.7)	1 (12.5)	2 (14.3)
Patient Summary			
KRAS Mutation	DDDDV 13D	DDDDRVVV	
Dose Limiting Toxicity	0	0	0
Biomarker Reduction / Clearance	2 / 5 (40)	5 / 7 (71)	7 / 12 (58) [b]
T cell Response	6 / 6 (100)	5 / 5 (100)	11 / 11 (100) [c]

TEAE: Treatment Emergent Adverse Event
[a] Preferred terms per the Medical Dictionary for Regulatory Activities, version 25.0
[b] Measured among 12 evaluable patients as of the data cut off: December 18, 2023
[c] Measured among 11 evaluable patients as of the data cut off: December 18, 2023

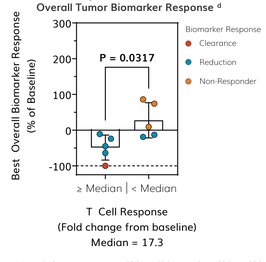
- No treatment-related SAEs, no dose-limiting toxicities, no discontinuation of study drug due to AE, no CRS or T cell related side effects
- Infrequent observation of injection site reaction, common vaccine associated AEs (fatigue, malaise), all grade 1-3
- Safety is consistent with prior ELI-002 2P observations[12] with improved T cell response

Tumor Biomarker Reductions in All KRAS Mutations Enrolled, Correlate with T Cells

AMPLIFY-7P Waterfall Plot: Biomarker Reduction / Clearance [a]



T Cell Response Correlation to Best Overall Tumor Biomarker Response [d]



Strength of ELI-002 7P Induced mKRAS-specific T cell Response Correlated to Anti-tumor Biomarker Response

- 4.9 mg Dose Level: 5/7 (71.4%) with biomarker reduction, 1/7 (14.3%) with biomarker clearance (1 PDAC)
- Responses occurred for all mutations enrolled: G12D, V, R, and G13D
- Responses among patients with diverse HLA I and II haplotypes, suggesting potential for broad utility among mKRAS-driven solid tumor cancer patients

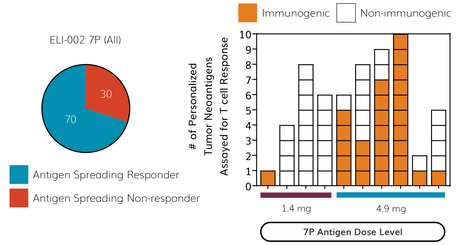
ELI-002 7P Monotherapy Pharmacologic Activity in High Relapse-risk PDAC and CRC

- Patients with above median T cell fold-change: 100% biomarker reduction / clearance observed
- Patients with below median T cell fold-change: 40% biomarker reduction, 60% non-response observed
- P-value = 0.0317 by Mann-Whitney test

[a] Measured among 12 evaluable patients as of the data cut off: December 18, 2023; [b] Literature reported mKRAS-presenting HLA I: A*02:01, A*03:01, A*11:01, A*30:01, A*66:01; B*07:02; C*01:02, C*03:03, C*03:04, C*08:02 [7,13-14]; [c] Literature reported mKRAS-presenting HLA II: DRB3*02, DRB1*01:01, DRB1*03:01, DRB1*07:01, DRB5*01; DPB1*03:01; DQA1*05:01, DQA1*05:05, DQB1*03:01 [7,13-14]; [d] Measured among 10 evaluable patients with both T cell and tumor biomarker assessments as of the data cut off: December 18, 2023

Antigen Spreading: T cells Targeting Personalized, Non-immunizing Tumor Neoantigens

AMPLIFY-7P Antigen-spreading T Cell Response: Non-mKRAS, Personal Tumor Neoantigen



ELI-002 7P Vaccination Induces Antigen Spreading: T Cell Responses Targeting Non-immunizing, Personalized Tumor Neoantigens

- Non-immunizing antigens from each patient's personal tumor mutanome were selected from whole exome sequencing and peptides were used to stimulate PBMCs directly ex vivo for assessment by Fluorospot and ICS. Immunogenic responses were defined with >2-fold increase over baseline level and >50 SFC per million PBMCs (Fluorospot) or >0.1% Cytokine+ (ICS)
- ELI-002 7P induced increased T cell responses targeting non-immunizing, personalized tumor neoantigens in 7/10 (70%) evaluable patients, 6/6 (100%) patients treated at the 4.9 mg RP2D dose level vs 1/4 (25%) at 1.4 mg dose level
- Observed responses included polyfunctional CD4 and CD8 T cell responses
- T cell responses were detectable by standard direct ex vivo IFNγ/Granzyme B Fluorospot and IFNγ/TNFα/IL2 intracellular cytokine staining, with no expansion required
- ELI-002 7P vaccination led to expansion of T cell responses targeting passenger mutations alongside mKRAS driver mutations in a majority of evaluable patients

Randomized, Controlled Phase 2 Study Ongoing for Adjuvant Treatment of PDAC

Randomized Phase 2

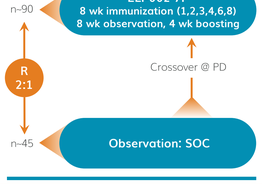
Monotherapy (no chemo, CPI combo)

- ✓ mKRAS: Expanded Antigen Coverage: G12D / V / R / C / A / S / G13D

Phase 2: Key Criteria

- ✓ Includes: mKRAS G12D / V / R / C / A / S / G13D
- ✓ Up front resectable Stage I, II or III disease (PDAC)
- ✓ Complete R0/R1 resection
- ✓ Radiographic NED status within 6 months following completion of locoregional treatment
- ✓ MRD agnostic (biomarker +/- included)

Schema



Endpoints

- Primary Endpoint: Disease-Free Survival
- Overall Survival
- Tumor Biomarker Response (in the biomarker subset)
- Safety
- iRECIST Overall Response Rate (in the crossover subset)
- Immunogenicity

TAKE HOME MESSAGES

Lymph node-targeted Therapeutic mKRAS-specific Cancer Vaccine ELI-002 7P:

- Safe and Well-tolerated, no Dose Limiting Toxicity, no CRS Observed
- Direct Ex Vivo Polyfunctional mKRAS-specific T cell Response Observed (100% Response)
- Data Show Frequent Anti-tumor Biomarker Reduction and Clearance
- T cell and Anti-tumor Biomarker Responses Observed for G12D, V, R, and G13D
- Frequent Antigen-spreading T Cell Responses to Personal non-mKRAS Tumor Neoantigens

- ✓ **RP2D 4.9 mg Antigen, 10 mg Adjuvant Dose Generates Improved mKRAS-specific T cell Responses** (100% Response, >8x Increased Median T cell Fold-change, 66.7% CD4 and CD8) and 100% Antigen Spreading Response
- ✓ **Strength of mKRAS-specific T cell Response Correlated to Tumor Biomarker Response**
- ✓ **Enrolling Randomized Phase 2 Study of Monotherapy ELI-002 7P in Adjuvant PDAC (NCT05726864),** DFS endpoint comparison to observation; Enrollment Expected to Complete in Q4 2024, Interim Analysis Expected in Q1 2025