ClinicalTrials.gov Identifier: NCT04853017 and NCT05726864 | Presented at the ASCO Annual Meeting, June 2-6, 2023, Chicago, IL, USA, and online | Abstract 2528 I Poster No. 370

AMPLIFY-201, a first-in-human safety and efficacy trial of adjuvant ELI-002 2P immunotherapy for patients with high-relapse risk KRAS G12D- or G12R-mutated pancreatic and colorectal cancer.

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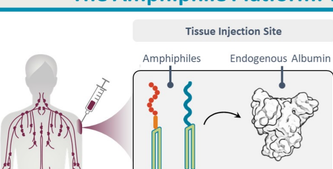
Why Target mutated KRAS with Therapeutic Vaccination?

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 naïve repertoire[7-8]
- **Promiscuous HLA presentation**: potential off-the-shelf use in diverse patient population[4-6]
- **Proven Clinical MOA**: mKRAS-specific T cells known to mediate anti-tumor efficacy[7-8]
- **Multi-targeting potential**: recognition of clonal and subclonal mKRAS variants to prevent escape[9]

HYPOTHESIS: mKRAS Vaccination will Prevent Tumor Recurrence in High Relapse-Risk Patients Following Standard Therapy

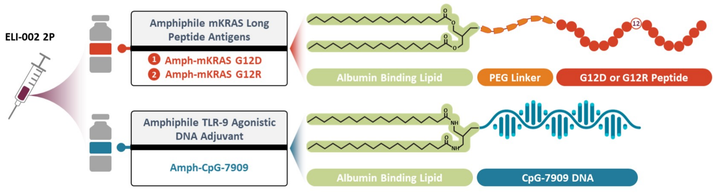
1 Technological Innovation: Amphiphile Lymph Node Targeting Platform[10-11]

- **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 **prevents 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**

Designing a Therapeutic Vaccine Targeting mKRAS: ELI-002 2P



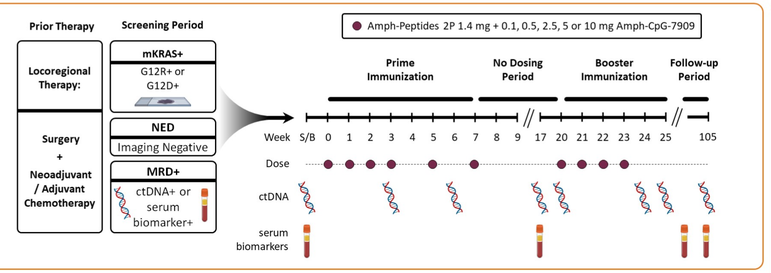
- Inclusion of **18-mer G12D and G12R mKRAS peptides** allows for delivery of **diverse HLA I and II –restricted epitopes** for presentation on varied patient HLA molecules
- **Amphiphile (Amph)-modification of peptides** promotes binding to endogenous albumin at the injection site to promote collection 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

The Amphiphile Platform: Targeting the Lymph Nodes[10-11]

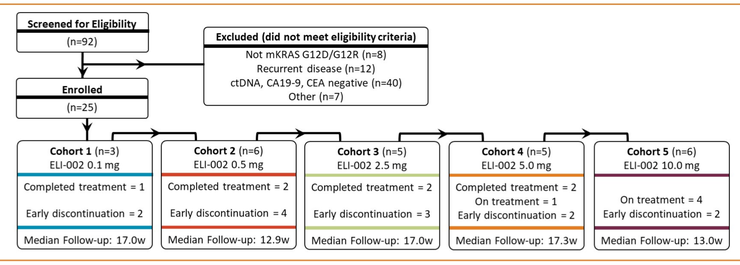
- **Conventional vaccine components** (e.g. peptide antigens and molecular adjuvants) are rapidly absorbed into blood capillaries after administration leading to **poor delivery to lymph nodes where protective immune responses are orchestrated.**
- **Amph-modification promotes albumin binding to reprogram 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 **prevents systemic exposure to avoid toxic effects of potent adjuvants.**

AMPLIFY 201: Prevention of Relapse in High-risk PDAC and CRC

Schema



Disposition



Demographics and Baseline Characteristics

	Cohort 1 (0.1 mg) n=3	Cohort 2 (0.5 mg) n=6	Cohort 3 (2.5 mg) n=5	Cohort 4 (5.0 mg) n=5	Cohort 5 (10.0 mg) n=6	Overall n=25
Age (years)						
Median	50.0	54.5	67.0	67.0	59.0	61.0
Range	47–61	37–69	63–77	47–75	48–69	37–77
Female Sex, n (%)	2 (66.7)	5 (83.3)	4 (80.0)	3 (60.0)	1 (16.7)	15 (60.0)
BMI (kg/m²)						
Median	25.2	22.1	22.3	23.3	26.2	23.4
Range	20.5–32.2	16.5–38.0	19.9–24.6	16.0–31.1	19.1–33.3	16.0–38.0
Race, n (%)						
Asian	0	1 (16.7)	0	0	1 (16.7)	2 (8.0)
White	2 (66.7)	5 (83.3)	4 (80.0)	5 (100)	5 (83.3)	21 (84.0)
Not reported	1 (33.3)	0	2 (20.0)	0	0	2 (8.0)
ECOG PS, n (%)						
0	3 (100)	4 (66.7)	4 (80.0)	2 (40.0)	5 (83.3)	18 (72.0)
1	0	2 (33.3)	1 (20.0)	3 (60.0)	1 (16.7)	7 (28.0)
Initial Diagnosis, n (%)						
PDAC	1 (33.3)	4 (66.7)	5 (100)	4 (80.0)	6 (100)	20 (80.0)
CRC	2 (66.7)	2 (33.3)	0	1 (20.0)	0	5 (20.0)
Disease Stage at Screening						
Stage I, II	1 (33.3)	2 (33.3)	3 (60.0)	1 (20.0)	1 (16.7)	8 (32.0)
Stage III, IV [a]	2 (66.7)	4 (66.7)	2 (40.0)	4 (80.0)	5 (83.3)	17 (68.0)
Prior Anti-cancer:						
Systemic therapy	3 (100)	6 (100)	5 (100)	5 (100)	6 (100)	25 (100)
Surgery/ Procedure	3 (100)	6 (100)	5 (100)	5 (100)	6 (100)	25 (100)
Radiation therapy	2 (66.7)	1 (16.7)	1 (20.0)	2 (40.0)	1 (16.7)	7 (28.0)

BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; PS: performance stats
[a] Resected oligometastatic (< 3 lesions) with NED on imaging was permitted

- **No treated related SAEs, no dose-limiting toxicities**, no discontinuation of study drug due to AE
- **Amph-CpG-7909 was safe** over a 100-fold range (0.1 – 10 mg); no T cell-related side effects
- Injection site reactions, grade 1 and 2, were observed

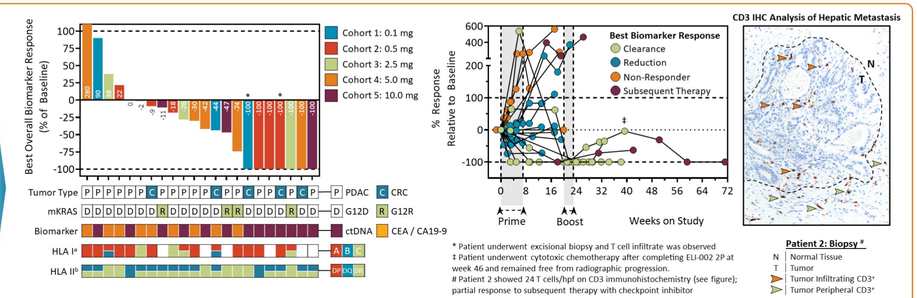
Adverse Events and Patient Summary

	Cohort 1 (0.1 mg) n=3	Cohort 2 (0.5 mg) n=6	Cohort 3 (2.5 mg) n=5	Cohort 4 (5.0 mg) n=5	Cohort 5 (10.0 mg) n=6	Overall n=25
Adverse Event Term [a]						
Patients with Any Related TEAE, n (%)	1 (33.3)	3 (50.0)	2 (40.0)	3 (60.0)	2 (33.3)	11 (44.0)
Injection site reaction	0	1 (16.7)	1 (20.0)	1 (20.0)	0	3 (12.0)
Fatigue	0	1 (16.7)	2 (40.0)	0	1 (16.7)	4 (16.0)
Headache	1 (33.3)	1 (16.7)	0	0	1 (16.7)	4 (16.0)
Asthma	0	0	0	0	1 (16.7)	1 (4.0)
Dyspnea	0	0	0	0	1 (16.7)	1 (4.0)
Nausea	1 (33.3)	0	0	1 (20.0)	0	2 (8.0)
Diarrhea	0	0	0	0	1 (16.7)	1 (4.0)
Anemia	1 (33.3)	0	0	0	0	1 (4.0)
Contusion	1 (33.3)	0	0	0	0	1 (4.0)
Dry skin	0	1 (16.7)	0	0	0	1 (4.0)
Herpes simplex reactivation	0	1 (16.7)	0	0	0	1 (4.0)
Hot flush	0	1 (16.7)	0	0	1 (16.7)	2 (8.0)
Myalgia	0	0	0	1 (20.0)	0	1 (4.0)
Nasal congestion	0	1 (16.7)	0	1 (20.0)	0	2 (8.0)
Lymphadenopathy	0	0	0	0	1 (16.7)	1 (4.0)
Pruritus	0	0	0	1 (20.0)	0	1 (4.0)
Patient Summary						
KRAS Mutation	DDD	DDDDDD	DRDDD	DDRDD	RRDDRD	
Dose Limiting Toxicity	0	0	0	0	0	0
Biomarker Reduction / Clearance	2 (67)	5 (83)	3 (60)	4 (80)	3 (100) [b]	17 (77) [c]
T cell Response	2 (67)	5 (83)	4 (80)	5 (100)	4 (100) [d]	20 (87) [e]

TEAE: Treatment Emergent Adverse Event
[a] Preferred terms per the Medical Dictionary for Regulatory Activities, version 25.0
[b] Measured among 3 evaluable patients
[c] Measured among 22 evaluable patients
[d] Measured among 4 evaluable patients
[e] Measured among 23 evaluable patients

Monitoring Early Relapse via Tumor Biomarkers: ctDNA / Serum Tumor Antigen

Tumor ctDNA / Serum Tumor Antigen

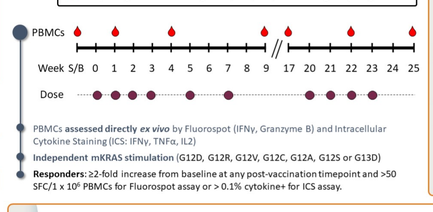


* Patient underwent excisional biopsy and T cell infiltrate was observed
‡ Patient underwent cytotoxic chemotherapy after completing ELI-002 2P at week 46 and remained free from radiographic progression.
# Patient 2 showed 24 T cells/hpf on CD3 immunohistochemistry (see figure); partial response to subsequent therapy with checkpoint inhibitor

[a] Literature reported mKRAS-presenting Class I alleles: A*02:01, A*03:01, A*11:01, A*30:01, A*86:01; B*07:02; C*01:02, C*03:03, C*03:04, C*08:02
[b] Literature reported mKRAS-presenting Class II alleles: 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

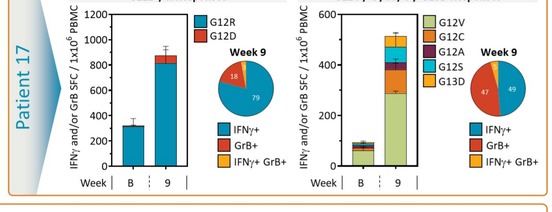
- **ELI-002 2P Monotherapy pharmacologic activity** in high relapse-risk PDAC and CRC with **17/22 (77.3%) biomarker reduction**, **7/22 (31.8%) biomarker clearance** (4 PDAC, 3 CRC)
- Responses occurred for both G12D and G12R and among **Patients with and without known Class I mKRAS-restricting HLAs,** suggesting potential for broad utility among mKRAS-driven solid cancer patients

Expansion of mKRAS-specific Immune Responses by ELI-002 2P Immunization

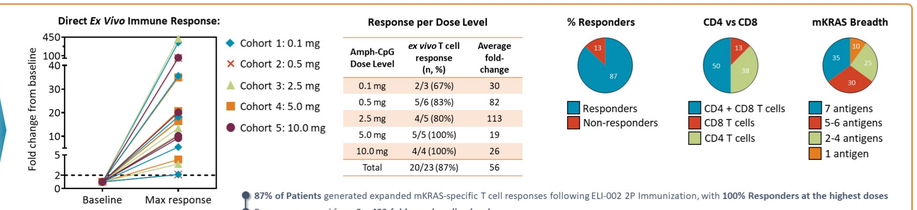


- PBMCs **assessed directly *ex vivo*** by Fluorospot (IFNγ, Granzyme B) and Intracellular Cytokine Staining (ICS: IFNγ, TNFα, IL2)
- **Independent mKRAS stimulation** (G12D, G12R, G12V, G12C, G12A, G12S or G13D)
- **Responders:** ≥2-fold increase from baseline at any post-vaccination timepoint and >50 SFC/1 x 10^6 PBMCs for Fluorospot assay or > 0.1% cytokine+ for ICS assay.

Patient 17



All Patients



Response per Dose Level

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

- **87% of Patients** generated expanded mKRAS-specific T cell responses following ELI-002 2P Immunization, with **100% Responders at the highest doses**
- Responses ranged from **2 – 423-fold over baseline levels**
- **CD4 and CD8 T cell responses were observed**, with 50% generating mixed CD4 + CD8 responses
- Patients generated **broad responses targeting multiple mKRAS antigens** beyond the immunizing epitopes G12D and G12R

TAKE HOME MESSAGES

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

- Safe and Well-tolerated, no Dose Limiting Toxicity, no CRS
- High Proportion with Tumor Biomarker Reduction (77%) & Clearance (32%)
- Induced Robust Polyfunctional T cell Responses Directly ex vivo (87% Response)

✓ **Follow-up for Patients treated with ELI-002 2P: Biomarker response / DOR / RFS / OS**

✓ **Open Phase 1, randomized Phase 2 Study of ELI-002 7P will expand mKRAS antigen coverage (NCT05726864) in PDAC, CRC, NSCLC patients: G12D, R, V, C, A, S, G13D**

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Acknowledgements and Disclosures

- We are grateful to the patients who participated in the study, their families, and the investigators and staff at the participating institutions.
- For author disclosures please refer to the abstract.

Funding

Elicio Therapeutics